IMMUNOHISTOCHEMICAL SPECTRUM

OF OVARIAN NEOPLASMS

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I hereby declare that the thesis entitled **"IMMUNOHISTOCHEMICAL SPECTRUM OF OVARIAN NEOPLASMS**" submitted towards partial fulfillment of the requirements for the award of **MD PATHOLOGY** degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. Harpreet Kaur**, Professor & Head, Department of Pathology, **Dr. Aminder Singh**, Associate Professor, Department of Pathology and **Dr. Kunal Jain** Assistant Professor Department of Oncology. No part of this thesis has formed the basis for the award of any degree previously.

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LIST OF ABBREVIATIONS

IHC	Immunohistochemistry
LGSC	Low grade serous carcinoma
HGSC	High grade serous carcinoma
WHO	World Health Organization
LGESS	Low grade endometrial stromal sarcoma
HGESS	High grade endometrial stromal sarcoma
EMA	Epithelial membrane antigen
WT1	Wilms' tumour 1
ER	Estrogen receptor
PR	Progesterone receptor
CK	Cytokeratin
SMA	Smooth muscle actin
HCG	Human chorionic gonadotropin
AFP	Alpha fetoprotein
LDH	Lactate dehydrogenase
TTF1	Thyroid transcription factor 1
MUC	Mucin
CEA	Carcinoembryonic antigen
BT	Brenners tumour
PAX 8	Paired- box gene 8
SF-1	Steroidogenic factor 1
PLAP	Placental alkaline phosphatase
CD 117	Cluster of differentiation 117
GATA 3	GATA binding protein 3
p63	Transformation related protein 63
p53	Transformation related protein 53
CCC	Clear cell carcinoma
TM	Thrombomodulin
SALL 4	SAL like protein 4
OCT 4	Octamer binding transcription factor 4
CD10	Common acute lymphoblastic leukemia antigen

CDX2	Caudal – type homeobox 2
FOXL 2	Forkhead box 2
Melan A	Melanocyte- differentiation- antigens MART-1
SOX 2	Sex determining region Y-box 2
NANOG	Homeobox protein NANOG
YST	Yolk sac tumour
EOT	Epithelial ovarian tumour
HPF	High Power Field

ABSTRACT

Introduction - Ovarian cancer is the sixth most common cancer and the seventh leading cause of cancer deaths among women worldwide with worst prognosis among all gynaecological malignancies. Ovarian tumours are heterogenous so an accurate histopathological diagnosis is required. World Health Organization classifies ovarian tumours as per their most probable cell of origin and histomorphological features. Immunohistochemistry is helpful where the morphology does not allow definite diagnosis of tumour

Aim and objectives - To study immunohistochemical spectrum of ovarian neoplasms.

Material and methods - Study was conducted in DMCH, Ludhiana from 1st March 2020 to 28th February 2022, for two years. All primary and secondary ovarian neoplasms undergoing immunohistochemistry for definite categorization were included in the study. The ovarian neoplasms which did not undergo immunohistochemistry test and all other neoplasms were excluded from the study. A total of 20998 specimens were received during this study period out of which 198 were ovarian neoplasms and on 88 cases of ovarian neoplasms immunohistochemistry was done.

Results – After immunohistochemistry was done, all the tumours were classified according to the WHO classification 2020 for ovarian neoplasms. Epithelial tumours formed the largest group with 56 cases (63.7%). Second most common type were sex cord stromal tumours comprising of 15 cases (17.0%) followed by metastatic tumours in 10 cases (11.3%), germ cell tumours 6 cases (6.8%). Least common were mesenchymal tumours comprising of 1 case (1.2%).

Conclusion – Immunohistochemistry is a useful adjunct to histopathology in diagnosis of ovarian tumours where morphological features overlap.

Key words - ovarian tumors, immunohistochemistry, histomorphology

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Keys of Masterchart

GPE	General physical examination
LFT	Liver function test
RFT	Renal function test
LN	Lymph nodes
NA	Not available
NG	Not given
ND	Not done
N	Negative
P	Positive
TM	Tumour
IX	Individual
VN	Vesicular nuclei
PN	Prominent nucleoli
HN	Hyperchromatic nuclei
ICN	Inconspicuous nucleoli
MOD	Moderate
MF	Mitotic figures
FT	Fallopian tubes
FC	Fibrocollagenous stroma
NP	Nuclear pleomorphism
DC	Dystrophic calcification
LP	Lamina propria
B/L	Bilateral
LVI	Lymphovascular invasion
PNI	Perineural invasion

INTRODUCTION

Ovaries are a pair of intraperitoneal organs located on either sides of uterus, which are suspended via ligaments. These are covered by a single layer of ovarian surface epithelium or germinal epithelium, underneath which is present tunica albuginea. Ovarian stroma is divided into cortex and medulla. Ovarian cortex contains follicles in varying stages of development.[1,2] Ovaries produce female sex hormones the estrogen and progesterone.[3]

Ovarian cancer is the 6th most common cancer and 7th leading cause of cancer deaths among females worldwide. In India, as per populationbased cancer registries ovarian cancer is the 3rd leading cancer, trailing behind cervix and breast cancer in women.[4] It has got the worst prognosis among all gynecological cancers. The overall 5 year survival is around 45%, primarily due to the late stage diagnosis of the disease.[5]

World Health Organization classifies the ovarian tumours on the basis of origin only, with most tumours falling under categories of epithelial, mesenchymal, sex cord stromal and germ cell tumours. The remaining tumours are in the miscellaneous category. As per the recently updated World Health Organization classification 2020, some modifications have been incorporated. These changes are regarding the grades of serous carcinomas, their origin and mutations. They have discussed regarding the mutations found in sex cord stromal tumours and small cell carcinoma. Recategorization of seromucinous carcinoma and reintroduction of gyandroblastoma in the updated WHO classification of ovarian tumours has been done.[6-10]

Ovarian tumours are characterized by vast heterogeneity in their clinical presentation, so an accurate morphological diagnosis is needed. World Health Organization classifies ovarian tumours as per their most probable cell of origin and histomorphology.[11] Out of these, 65% are surface epithelial tumours, followed by 15% germ cell tumours, 10% sex cord stromal tumours. Metastatic tumours to ovaries

comprise of 5% tumours. Miscellaneous tumours form another group in classification. Of the surface epithelial tumours most common are serous tumours and serous carcinomas are the most common malignant neoplasms.

Although, the concept of immunohistochemistry [IHC] has been known since the 1930s, the first IHC study was published in 1942. The basic idea behind IHC is that specific antibodies are used to demonstrate antigen within tissue sections. Immunohistochemical markers, in addition to relevant clinical data, imaging techniques, histomorphological findings, have become necessary for a precise diagnosis and subtyping of ovarian neoplasms. The present study was undertaken to classify the ovarian tumours according to WHO 2020 and to study the various immunohistochemistry markers in them.

Immunohistochemistry is extremely useful in a large number of cases where morphology and clinical features alone do not lead to a definite diagnosis.[12] As per the cell of origin, epithelial tumours derived from surface epithelium are immunoreactive for keratin, EMA, CA 125, vimentin, estrogen receptors, progesterone receptors, WT1 and p53. Sex cord stromaltumours derived from stroma composed of spindled cells resembling fibroblasts surrounded by reticulin are immunoreactive for FOXL2, ER, SF-1, inhibin and calretinin. Granulosa cells lack reticulum around them and stain for vimentin, FOXL2 and show variable or weak staining for keratins.[2] Germ cell tumours are immunoreactive for CD117, PLAP, AFP and other markers. Metastatic tumours are immunoreactive for specific immunohistochemical markers depending on the site of origin. Immunohistochemistry technique is widely used in diagnostics and research, and its applications continue to be extended due to its easy utility, reliability and versatility. Immunohistochemistry is now used not only for diagnosis but also for prognosis, microscopic tumour staging, response to therapy and for selection of therapeutic agents.[13]

Immunohistochemistry finds a specific utility in ovarian tumours because of diversity of diagnosis and often subtle nature of diagnostic criteria. Also the use of increasingly small amounts of tissue for diagnosis highlights the significance of this method. Nowadays, immunohistochemistry has become a gold standard method of diagnosis for surgical pathology.[13]

AIMS AND OBJECTIVES

To study immunohistochemical spectrum of ovarian neoplasms.

REVIEW OF LITERATURE

Ovaries are a pair of intraperitoneal pelvic organs located on either sides of the uterus near the lateral pelvic wall, behind the broad ligament, and anterior to the rectum. Before puberty, ovarian surface is smooth. However, its surface becomes irregular with ovulations. Every ovary has two borders and two surfaces. The mesovarium connects them to the broad ligament, the ovarian ligament to the uterine cornu, and the infundibulopelvic ligament to the lateral pelvic wall. [1,2]

Their average size during the reproductive period is 4x2x1 centimeters and their average weight is 5 to 8 grams. However, after menopause they shrink to half or less of this size. The ovarian lymph vessels drain into large trunks that form a plexus at hilum, from where they drain into para-aortic nodes through mesovarium. Others drain to the external and internal iliac, common iliac, and inguinal nodes.

A single layer of modified mesothelium is covered by ovarian surface epithelium or geminal epithelium. Tunica albuginea forms the capsule of ovary that lies beneath the germinal epithelium. The ovarian substance is divided into two parts: outer cortex and inner medulla.The inner medulla contains loose connective tissue, neurovascular tissue and lymphatics. The outer cortex contains ovarian follicles and connective tissue. During reproductive years, in females ovarian cortex is the site of ovarian cycle. It has ovarian follicles in varying stages of development. Oogenesis is the formation of gametes in ovaries, and folliculogenesis is the development of ovarian follicles. Morphology and morphometry of an ovarian follicle vary at different stages of life-prenatal, prepubertal, reproductive, and menopausal.[2]

Keratin, epithelial membrane antigen (EMA), Ber-EP4, CA 125, vimentin, oestrogen and progesterone receptors (ER and PR), and follicle-stimulating hormone are all immunoreactive with the ovarian epithelium. In the cortex, epithelial inclusion glands/cysts are common. Boundaries between cortex and medulla of ovarian stroma are not distinct. It is primarily made up of spindle-shaped stromal cells

that resemble fibroblasts and are typically arranged in whorls or a storiform pattern. The cells are surrounded by a dense network of reticulin fibres and may contain cytoplasmic lipid. They are immunoreactive for ER, PR and FOXL2.[1] Some of these cells have myoid characteristics and are immunoreactive for SMA and desmin. Also found in the ovarian stroma are luteinized cells, decidual cells, nests of cells resembling endometrial stromal cells, mature fat cells, and neuroendocrine cells.

The ovarian follicle has a life cycle that includes primordial, maturing (primary, secondary, tertiary, and graafian), and atretic forms, as well as corpora lutea and corpora albicantia for those that have reached full maturity. Primordial follicles contain germ cells that have migrated into the ovary from the yolk sac endoderm and developed into oogonia and oocytes. The oocyte, the granulosa layer, and the two theca layers comprise the maturing follicle. Granulosa cells lack a reticulum and are immunoreactive for vimentin, FOXL2, and ER, as well as variable to weak immunoreactivity for keratin.[1] They have small rosette like formations known as Call-Exner bodies, which contain a deeply eosinophilic filamentous material made up of excess basal lamina at their centre. Theca cells derived from the stroma form an internal layer (which is typically luteinized) and an external layer (which is very cellular and can simulate a neoplastic process).[2]

Understanding the development and anatomy of the ovary is crucial to comprehend the tumours that arise in this complex organ. The female genital tract develops normally through a series of strictly regulated events involving primordial germ cells, the mullerian (paramesonephric) ducts, the wolffian (mesonephric) ducts, and the urogenital sinus.

• By the fourth week of pregnancy, germ cells appear in the yolk sac wall. They migrate into the urogenital ridge by the fifth or sixth week and stimulate proliferation of the mesodermal epithelium, which gives rise to the ovarian epithelium and stroma.

• Around the sixth week of development, the lateral mullerian ducts form through invagination and fusion of the coelomic lining epithelium. The ducts grow caudally into the pelvis, where they swing medially to join the urogenital sinus at the mullerian tubercle. These fused ducts come into contact with the urogenital sinus as they grow caudally. The unfused upper mullerian ducts develop into the fallopian tubes, while the fused lower portion becomes the uterus, cervix, and upper vagina.

• Urorectal septum divides the cloaca to form the urogenital sinus. It then forms the lower part of vagina and external genital vestibule. In females mesonephric ducts normally regress, but remnants may persist into adulthood as epithelial inclusions. These rests in the cervix and vagina can be cystic and are known as Gartner duct cysts. The epithelial lining of the and the ovarian surface share a common origin from coelomic epithelium, which may explain why morphologically similar benign and malignant lesions arise in various sites within the female genital tract and adjacent peritoneal surfaces.

The female gametes, oocytes, are produced by the ovaries and develop into ova after fertilisation. They produce the female sex hormones progesterone and oestrogen, which are required for ovarian cycle, fertilisation and pregancy.[3]

In women worldwide, ovarian cancer is the sixth most common cancer and the seventh leading cause of cancer deaths. Ovarian cancer is the third most common cancer among women in most population based cancer registries in India, trailing only cervix and breast cancer.[4] Ovarian cancer has the poorest prognosis of any gynaecological cancer. Owing primarily to the disease's late stage at diagnosis, the overall 5-year survival rate is around 45%.[5]

Ovarian tumours are classified primarily morphologically and based on the cytological characteristics of the tumour cells. Immunohistochemistry backs up this morphology based classification system, demonstrating that it accurately reflects histogenesis/cell of origin as well as the underlying molecular abnormalities.

WHO classifies the ovarian tumours solely on the basis of origin (primary), with the majority of tumours falling into the epithelial, mesenchymal, sex cord stromal, and germ cell categories. The remaining tumours are classified as miscellaneous.

As per the recently updated WHO Classification 2020 the ovarian tumours are classified under the following categories:

- Epithelial tumours
- Serous tumours

Serous cystadenoma, adenofibroma and surface papilloma
Serous borderline tumour
Low grade serous carcinoma
High grade serous carcinoma

- Mucinous tumours

Mucinous cystadenoma and adenofibroma
Mucinous borderline tumour
Mucinous carcinoma

- Endometrioid tumours

Endometrioid cystadenoma and adenofibroma
Endometrioid borderline tumour
Endometrioid carcinoma

- Clear cell tumours

Clear cell cystadenoma and adenofibroma
Clear cell borderline tumour
Clear cell carcinoma

- Seromucinous tumours

Seromucinous cystadenoma and adenofibroma
Seromucinous borderline tumour

- Brenner tumours

Brenner tumour
Brenner tumour, borderline malignancy
Brenner tumour, malignant

- Other carcinomas

Mesonephric-like adenocarcinoma

Undifferentiated and dedifferentiated carcinoma

Carcinosarcoma

Mixed cell adenocarcinoma

- Mesenchymal tumours

Leiomyoma NOS

Smooth muscle tumour of uncertain malignant potential

Leiomyosarcoma NOS

Endometrioid stromal sarcoma, low grade

Endometrioid stromal sarcoma, high grade

Ovarian myxoma

- Mixed epithelial and mesenchymal tumours

Adenosarcoma

- Sex cord stromal tumours
- Pure stromal tumours

FibromaNOS

Cellular fibroma

Thecoma NOS

Thecoma, luteinized

Sclerosing stromal tumour

Microcystic stromal tumour

Signet ring stromal tumour

Leydig cell tumour NOS

Steroid cell tumour, NOS

Steroid cell tumour, malignant

Fibrosarcoma NOS

- Pure sex cord tumours

Adult granulosa cell tumour

Granulosa cell tumour, juvenile

Sertoli cell tumour, NOS

Sex cord tumour with annular tubules

- Mixed sex cord stromal tumours

Sertoli-Leydig cell tumour NOS

Sertoli-Leydig cell tumour, well differentiated

Sertoli-Leydig cell tumour, moderately differentiated

Sertoli-Leydig cell tumour, poorly differentiated

Sertoli-Leydig cell tumour, retiform

Sex cord stromal tumour, NOS

Gynandroblastoma

- Germ cell tumours

Teratoma, benign

Immature teratoma, NOS

Dysgerminoma

Yolk sac tumour

Embryonal carcinoma NOS

Choriocarcinoma NOS

Mixed germ cell tumour

- Monodermal teratomas and somatic type tumours arising from a dermoid cyst

Struma ovarii NOS

Struma ovarii, malignant

Strumal carcinoid

Teratoma with malignant transformation

Cystic teratoma NOS

- Germ cell sex cord stromal tumours

Gonadoblastoma

Dissecting gonadoblastoma

Undifferentiated gonadal tissue

Mixed germ cell - sex cord stromal tumour, unclassified

- Miscellaneous tumours [6]

Adenomas of rete ovarii

Adenocarcinoma of rete ovarii

Wolffian tumour

Solid pseudopapillary tumour of ovary

Small cell carcinoma of the ovary, hypercalcemic type
Small cell carcinoma of the ovary, large cell variant
Wilms tumour

- Metastasis

Major changes as per WHO Classification 2020 from WHO Classification 2016 are

• WHO first classified low and high grade serous carcinoma as different subtypes of the same tumour; now it is clear that these are two different types of carcinoma with different molecular characteristics, immunohistochemical profiles, morphology, pathogenesis, and tumour progression.

• The majority of highgrade serous carcinomas of the ovary develop from a precursor lesion known as serous tubal intraepithelial carcinoma in the distal fimbria of the fallopian tube (STIC).[7]

• Ovarian low grade serous carcinomas develop from benign or borderline serous neoplasms.

• SET (solid, endometrial-like, transitional) patterns have p53 mutations and are classified as high grade serous carcinoma.

• Many mutations have been discovered in sex cord stromal tumours that can distinguish subtypes such as adult granulosa cell tumour (FOXL2) from poorly differentiated Sertoli-Leydig cell tumours (DICER1) and microcystic stromal tumour (DICER1) (CTNNB1 or APC mutation).[8]

•SMARCA4 mutations are linked to hypercalcemic small cell carcinoma.[9]

• Seromucinous carcinoma has been removed and is now classified as an endometrioid carcinoma subtype.[10]

•After being removed from the previous WHO edition, gynandroblastoma has been reintroduced in the new WHO classification.

Because ovarian tumours have such a wide range of clinical manifestations, an accurate histopathological diagnosis is essential. The World Health Organization (WHO) categorises ovarian tumours based on their most likely cell of origin and histomorphological characteristics.[11] Immunohistochemistry is useful in many cases where morphology and clinical features alone do not allow a definite diagnosis of a tumour present in tissue sections.[12]

Immunohistochemistry is now used not only for diagnosis but also for prognosis, microscopic tumour staging, predicting response to therapy, and selecting therapeutic agents, as well as analysis of the IHC profile of ER, PR, Ki67, and p53 in various ovarian epithelial tumours, CD117, PLAP, AFP and other markers in various germ cell tumours, FOXL2, SF-1, and inhibin in various sex cord tumours. Neuroendocrine differentiation markers can help with the diagnosis of primary and metastatic neuroendocrine carcinomas, primitive neuroectodermal tumours (PNETs), and primary and secondary carcinoid tumours. In general, the most specific markers of neuroendocrine differentiation are chromogranin and synaptophysin. NSE and CD56 (neural cell adhesion molecule; NCAM) are less specific but more sensitive and should only be used for screening. The immunohistochemistry (IHC) technique is widely used in diagnostics and research, and its applications are expanding due to its ease of use, dependability, and versatility.

Immunohistochemistry (IHC) has evolved as the gold standard method of surgical pathology diagnosis. IHC is particularly useful in ovarian tumours due to the variety of diagnoses and the often subtle nature of diagnostic criteria. The use of increasingly small amounts of tissue for diagnosis, emphasises the significance of this method. With the introduction of new techniques, the sensitivity and crispness of IHC stains have gradually improved. IHC is a technique used to look for cell or tissue antigens. The technique is divided into two steps:

A: slide preparation (specimen fixation and tissue processing) and reaction stages (in order as given: antigen retrieval, non-specific site block endogenous peroxidase block, primary antibody incubation, and the employment of systems of detection, revealing and counterstaining and also slide mounting and storage).

B: interpreting and quantifying the obtained expression.[13]

The World Health Organization classifies ovarian tumours histologically according to the most likely tissue of origin: surface epithelial (65%), germ cell (15%), sex cord-stromal (10%), metastases (5%), and miscellaneous.

The majority of malignant tumours are surface epithelial in nature. A definitive diagnosis requires establishing a correlation between histomorphological features and immunohistochemistry findings wherever possible.

Epithelial tumours

Serous tumours

Benign serous tumours: Adenofibroma, serous cystadenoma, and surface papilloma - Tumours with epithelial cell types similar to those found in the fallopian tube, including ciliated cells. The epithelial component may be associated with a prominent component of stromal cells (cystadenofibroma, adenofibroma), absence of stromal cells (cystadenoma), or may be entirely a surface papillary lesion (surface papilloma). Combinations of these growth patterns are also possible. The patients' ages range from 40 to 60 years. Women are often asymptomatic. Macroscopically: A 1 cm cut-off size is used to distinguish cortical inclusion cysts from serous cystadenomas (> 1 cm). Cystic tumours have smooth external surfaces, range in size from 1 to > 30 cm, and contain one or more cysts conatiningwatery clear fluid. Cystadenofibromasare made up of cysts surrounded by fibrotic tissue. Surface papillomas are exophytic, whereas adenofibromas are solid.

Because these lesions are benign, the prognosis is good, though they may occasionally recur after cystectomy. [14]

Borderline serous tumour

SBTs are non-invasive tumours that have more epithelial proliferation and cytological atypia than benign serous tumours but less than low-grade serous carcinoma (LGSC). The average age of the patients is 42 years. Macroscopically, the tumours are larger than 5 cm in size and usually cystic. With a papillary tumour involving at least part of the cyst lining or representing the surface component, the external surface can be velvety. About one-third of patients have bilateral tumours. Microscopically, a hierarchical branching pattern is typical, with irregular papillae branching from large to progressively smaller papillae and terminating in detached tufts of epithelial cells. The papillae are lined by stratified or non-stratified cuboidal to columnar ciliated cells. Many tumours contain a variable number of polygonal and hobnail cells with eosinophilic cytoplasm, occasionally clear cytoplasm, moderately enlarged, hyperchromatic nuclei, and nucleoli. [15] Clusters of cells in the stroma with abundant eosinophilic cytoplasm measuring 5 mm in greatest dimension have been referred to as "microinvasion".[16] These cells have a significantly lower Ki67 index and are less likely to express oestrogen and progesterone receptors, indicating that they are terminally differentiated or senescent.[17]

Immunohistochemistry: Cytokeratin, EMA, WT1, and PAX8 are epithelial markers that are expressed. Both ER and PR frequently show strong staining. p53 shows a wild type staining pattern. There is no diffuse p16 staining.[18]

Serous borderline tumour

Micropapillary variant/ Non-invasive low-grade serous carcinoma: A non-invasive tumour with micropapillary and/or cribriform patterns composed of rounded cells with scant cytoplasm and moderate nuclear atypia and a nonhierarchical branching architecture. Micropapillae have inconspicous to scant stromal cores. In contrast to serous borderline

tumours (SBT), which have columnar cells that are frequently ciliated, the cells in these tumours are cuboidal to polygonal with a high nuclear to cytoplasmic ratio and small, uniform, more atypical nuclei. Eosinophilic nucleoli are visible, but cilia are conspicuously absent.[19] Immunohistochemistry is identical to that of serous borderline tumours.

Low grade serous carcinomas

Invasive carcinomas with distinct patterns that exhibit low-grade malignant cytological atypia. LGSC patients present nearly a decade earlier than HGSC patients. These patients usually present with ovarian masses or are detected by chance. In advanced stages of disease, ascites may occur. On imaging, ovarian masses are typically cystic, but they may contain thick septae or nodular components with increased vascularity. Macroscopically, LGSC is frequently bilateral and characterised by fine papillary growth. Necrosis is uncommon in comparison to HGSC. Calcification is common and widespread. Calcification can cause extra-ovarian lesions to feel gritty when touched.

Microscopically, a variety of architectural patterns, including single cells and irregularly shaped smallnests haphazardly infiltrating stroma, micropapillae or less commonly, macropapillae surrounded by an unlined clear space; different invasion patterns frequently coexist. [20] LGSC cells have mild to moderate nuclea atypia, a single prominent nucleolus, and are made up of a more uniform population of small cells with limited nuclear pleomorphism. Necrosis is almost non-existent, psammoma bodies are much more common, and mitotic activity is much lower (typically 2-3 mitotic figures per 10 HPF) than in HGSC. [21]

Immunohistochemistry: When compared to HGSC, the Ki-67 proliferation index is typically low.

High grade serous carcinoma

It is made up of epithelial cells with papillary, glandular, and solid patterns, as well as high-grade nuclear atypia. It typically manifests in

the sixth decade of life with symptoms such as nausea, anorexia, early satiety, abdominal distension, bloating, pain, and constipation, back pain, and urinary frequency. Serum CA-125 levels are typically elevated in advanced stage disease, with median values ranging from 500 to 1000 U/ml.[22] Macroscopically, tumours are frequently bilateral, exophytic, and exhibit solid and papillary growth as well as fluid-filled cysts. The solid regions are tan-white in colour and usually have extensive necrosis and haemorrhage. The fallopian tube may be involved macroscopically. Microscopically, HGSCs are composed of solid masses of cells with slit-like spaces. Papillary, glandular, and cribriform areas are also visible. Necrosis is common. Nuclei are large, hyperchromatic, and pleomorphic, with large bizarre or multinucleated forms occurring frequently. Nucleoli are typically eosinophilic and prominent. Mitoses are numerous and frequently abnormal. Psammoma bodies can be seen in a variety of ways.

Immunohistochemistry: WT1 nuclear expression is thought to be a useful marker for HGSC. p53 expression can show two distinct patterns that correlate with a TP53 mutation. The most common pattern observed is strong diffuse nuclear staining in 60% or more of cells. A missense mutation is associated with this pattern. The other pattern is complete staining absence, which corresponds to a nonsense mutation. Because mutated TP53 is found in nearly all HGSC, this stain is thought to be useful in confirming the diagnosis of an HGSC.

Mucinous tumours

Benign mucinous tumours

Mucinous cystadenoma/adenofibroma

It is a benign, cystic tumour lined by mucinous gastrointestinal-type epithelium or, less frequently, have an eminent fibrous stroma (adenofibroma). It typically manifests in the fifth decade, with the most common presenting symptoms being abdominal/pelvic pain and the presence of an abdominal or pelvic mass. Macroscopically, these are

unilateral (95%) with a smooth surface, multilocular, and occasionally unilocular, ranging in size from a few centimetres to 30 centimetres. Microscopically, it is made up of numerous cysts and glands that are lined by simple, non-stratified mucinous epithelium that resembles gastric foveolar-type or intestinal epithelium and contains goblet cells, neuroendocrine cells, and Paneth cells. There may be focal papillae visible.

Mucinous borderline tumours

These are made up of mild to moderately atypical gastrointestinal-type, mucin-containing epithelial cells that proliferate more than benign mucinous tumours. Stromal invasion is not present. Macroscopically, the tumour ranges in size from a few centimetres to 50 cm.[23] The tumours are almost always unilateral and have a smooth external surface with small to large cysts with mucinous areas and some solid areas. The cysts are lined by gastrointestinal type epithelium with varying degrees of stratification, tufting, and villous or slender filiform papillae. The cells have mild to moderate nuclear enlargement, hyperchromasia, and occasionally pseudostratification, but no high-grade nuclear features are visible. The mitotic index ranges from mild to intense.[24] About 20% of tumours have Pseudomyxoma ovarii (acellular pools of mucin in the stroma). Immunohistochemistry:

CK7 is typically diffusely positive, whereas CK20 exhibits variable positivity (usually less extensive than CK7 expression). CDX2 expression varies, ER and PR are almost always negative, and PAX8 is expressed in up to 50% of tumours. [25]

Mucinous carcinomas

It is a type of malignant epithelial tumour made up of gastrointestinal-type cells with intracytoplasmic mucin. Mucinous carcinoma is responsible for 3-4% of all primary ovarian carcinomas.[26] The average age at presentation is 45 years, and the patient complains of abdominal swelling or pain. At the time of presentation, the majority of tumours are confined to the ovary. Macroscopically, Mucinous

carcinomas form large, unilateral, complex, solid, and cystic masses. In most cases, there is no evidence of surface involvement. Microscopically, there is a spectrum of architectural and cytological atypia that includes areas that are benign, borderline, and clearly carcinomatous. Invasive carcinoma is distinguished by two distinct invasion patterns, which may coexist in a single tumour. Marked glandular crowding with little intervening stroma creates a labyrinthine appearance in the confluent glandular or expansile invasive pattern. A cribriform pattern is also noted. A less common destructive stromal invasive pattern is distinguished by irregular glands, nests and single cells with malignant cytological features infiltrating stroma, which is frequently desmoplastic. Mitotic activity is frequently high, and abnormal mitotic figures are common.

Immunohistochemistry: CK7 is typically diffusely positive in immunohistochemistry, whereas CK20 exhibits variable positivity (usually less extensive than CK7 expression). CDX2 expression varies, ER and PR are almost always negative, and PAX8 is expressed in up to 50% of tumours.[25]

Endometrioid tumours

Benign endometrioid tumours

Endometrioid cystadenoma/adenofibroma

An endometrioid cystadenoma is a cystic lesion lined by benign endometrioid type epithelium that lacks the stroma, typical vasculature, and other features of endometriosis. When accompanied by a dense fibromatous component, the tumour is classified as an endometrioid adenofibroma. Endometriotic cysts are associated with haemorrhage and are lined by endometrial epithelium which overlies endometrial stroma. Many small blood vessels are found in the endometrial stroma. There are also haemosiderin-laden macrophages and fibrosis.

Endometrioid borderline tumour

A solid or cystic tumour made up of crowded glands lined by atypical endometrioid-type cells and devoid of destructive stromal invasion and/or confluent glandular growth. Macroscopically: They are 9 cm in diameter, on average. Tumours are usually solid, but they can also be cystic. Friable tumours involving the cyst lining are common in cystic tumours. The cyst fluid is brownish, with the appearance of haemorrhage. Solid tumours are associated with dense fibromatous stroma. Microscopically: It is characterised by crowded, back-to-back endometrioid glands with mild to moderate cytological atypia, often with epithelial stratification.

Endometrioid carcinoma

It is the second most common type of ovarian epithelial malignancy, accounting for 10-15% of all ovarian carcinomas. It occurs most frequently in the fifth and sixth decades of life. Endometriosis in the same ovary or elsewhere in the pelvis is found in 42% of cases.[27] Ca-125 levels are elevated in approximately 80% of cases. Macroscopically, the average size is 15 cm, with a smooth outer surface. Friable soft masses or papillae partially filling cystic spaces that may contain blood-stained fluid are visible on the cut surfaces. They can be completely solid or show signs of haemorrhage or necrosis. Microscopically: These tumours have glands arranged back toback, with confluent or cribriform patterns of round, oval, tubular glands or villoglandular patterns. The glands are lined by non-mucin-containing stratified epithelium with well-defined luminal margins. Tumours can grow destructively, with stromal invasion in the form of glands, cell clusters, or individual cells infiltrating the stroma disorderly.

Immunohistochemistry: PAX-8, ER, and PR are usually nuclear positive in tumour cells, while CK7 is cytoplasmic positive. WT-1 is found to be positive in 4% of cases.

Clear cell tumours

Benign clear cell tumours

Clear cell cystadenoma/ adenofibroma: A tumour made up of glands or cysts lined by bland cuboidal to flattened cells with clear or eosinophilic cytoplasm present in a fibromatous stroma. Cytologically, the nuclei of both the epithelial and stromal components are bland. Mitotic figures are uncommon to non-existent.

Clear cell borderline tumour

These are clear cell tumours with glandular epithelial atypia without stromal invasion. In a fibromatous stroma, the glands are typically round to oval and relatively evenly spaced.

Clear cell carcinomas

It is a malignant tumour made up of clear, eosinophilic and hobnail cells with tubulocystic, papillary, and solid patterns. The average patient age is 55 years. In 50-70 percent of cases, this tumour is caused by endometriosis. It has also been linked to Lynch syndromes.

Macroscopically: These tumours are usually unilateral and have a diameter of 15 cm. They can be solid, solid and cystic, or solid with fleshy, paleyellow nodules lining an endometriotic cyst. Microscopically: This tumour has a mixture of tubulocystic, papillary, and solid patterns. The papillae are usually regular and small, but they can be large and have prominent fibrovascular cores that are frequently hyalinized.[28] Sheets of polyhedral cells are separated by delicate septa to form solid areas. Tumour cells can be polygonal, cuboidal, or flattened, and the cytoplasm can be clear or, less commonly, eosinophilic. Hobnail cells can also be seen. Nuclei are hyperchromatic, often eccentric, and have prominent nucleoli. Mitotic figures are extremely rare. There are psammoma bodies and eosinophilic hyaline bodies visible.

Immunohistochemistry: The tumour cells express NapsinA and PAX8 but do not express WT-1.

Seromucinous tumours

Seromucinous cystadenoma/ adenofibroma

These benign tumours composed of a unilocular cyst with a smooth surface and inner lining. They could contain either serous or mucinous fluid. Endometrioid and, less frequently, transitional or squamous cells may be seen in the cysts, which are lined by a variable admixture of serous and mucinous cells (endocervical-type). The stroma, if present, is bland and fibromatous.

Seromucinous borderline tumour

A non-invasive, proliferative epithelial tumour made up of various epithelial cell types, most commonly serous and endocervical-type mucinous. Macroscopically: The average size is 8-10 cm. Up to 40% of cases are bilateral. These tumours are usually unilocular, smooth-surfaced, and filled with viscid fluid. Friable papillary excrescences can be seen occupying varying proportions of the cyst lining. Granular to haemorrhagic foci may be present, indicating an endometriosis connection. Microscopically: These tumours have architectural characteristics that are similar to serous borderline tumours. The epithelium lining the papillae is usually stratified and consists primarily of endocervical type mucinous or serous epithelium, though endometrioid and squamous epithelium are not uncommon. There are no goblet cells. Cytoplasmic eosinophilia is common, and the nuclei are low-grade; mitotic figures are uncommon.

Immunohistochemistry: CK7 in ciliated cells and CK20 in mucinous cells are common in these tumours. CDX2 is almost always negative. They typically express ER and PR, and the majority of tumours are negative for WT1.

Seromucinous carcinomas

According to update 2020 WHO classification of ovarian neoplasms now seromucinous carcinomas have been classified as a subtype of endometrioid carcinoma. Macroscopically: The average tumour size is 12 cm, and more than half of the tumours are bilateral. Tumours are either unilocular or multilocular, with solid areas. Papillary excrescences maybe found on the inner lining and surface of the cysts. Microscopically: Tumours are generally papillary and exhibit epithelial stratification similar to serous tumours. Although destructive infiltrative growth occurs, the most common pattern of invasion is cribriform and confluent (expansile). Endocervical mucinous and serous epithelium is found in these tumours. The mitotic index varies but is usually low. Immunohistochemistry: The immunohistochemical profile of borderline seromucinous tumours is similar.

Brenner tumour

Benign Brenner tumour

It is most common in people in their fifth to seventh decades of life, but it has also been observed in young females. Most of the time, it is asymptomatic. The majority of benign Brenner tumours are 2 cm in size and are mostly unilateral. Macroscopically: They are circumscribed and solid, with a firm rubbery consistency. The cut surface is either grey white or yellowish. In some cases, calcifications can be seen. Microscopically: Brenner tumours are benign and are distinguished by oval or irregular nests of transitional-type cells within a fibrous stroma. Nests can be solid or have central cavities filled with mucin or eosinophilic material. Transitional-type, mucinous, ciliated, cuboidal, or flat cells can line the lumina. Transitional cells are polyhedral to elongate in shape, with pale to clear cytoplasm. The nuclei are ovoid and covered in fine chromatin. Nucleoli may be visible, and nuclei may have longitudinal grooves in some cases.

Immunohistochemistry: Brenner tumours express CK7, p63, S100, GATA3, uroplakin, and thrombomodulin and focally express CK20.[29]

Borderline Brenner tumour

The papillary component is similar to non-invasive papillary transitional cell (urothelial) tumours of lowgrade type. In the absence of invasion, high-grade cytological features can be diagnosed as borderline Brenner tumour with intraepithelial carcinoma.

Immunohistochemistry: p63 and GATA3 immunohistochemical stains are usually positive. WT1 has always been negative.[29]

Malignant Brenner tumour

The tumour is made up of irregular masses of malignant transitional type cells. Within the tumour, cystic areas are lined by multilayered epithelium with hyperchromatic and pleomorphic nuclei and prominent mitotic activity. Because of the densely fibromatous background of the tumour, invasion may be difficult to detect, but a desmoplastic stromal reaction can aid in identifying unequivocal stromal invasion.

Immunohistochemistry: The immunoprofile is similar to that of benign Brenner tumours, but the invasive component has a variable pattern of expression.

Undifferentiated carcinomas

A malignant, aggressive epithelial tumour with no specific differentiation of any type of Mullerian cell. These tumours typically have sheet like growth and are frequently associated with geographic necrosis. Undifferentiated carcinoma immunophenotype is poorly defined. These carcinomas show epithelial markers like EMA and CK. They are usually CK focal positive.

Sex cord Stromal tumours

Fibromas

These benign stromal tumours are made up of spindled to ovoid fibroblastic cells that produce collagen. It is most common in the fourth decade of life, but it can occur at any age and is bilateral if associated with Gorlin syndrome. The majority of these tumours are unilateral.

Meigs syndrome is thought to occur in 1% of cases. Macroscopically: The ovarian capsule is typically smooth and intact, and the cut section is hard, chalky, white or yellowish white. Oedema and cystic degeneration may be present, particularly if the tumour is large. Torsion-induced haemorrhage or necrosis can occur. Fibromas are made up of cells with spindled to ovoid bland nuclei and scant cytoplasm. The cells are arranged in intersecting bundles, forming a storiform pattern.

Immunohistochemistry: Fibromas may be immunoreactive for inhibin, calretinin, FOXL2, and CD56, as well as a patchy weak positive for WT1.[30,31]

Thecomas

These tumours are mostly unilateral and affect postmenopausal women. Thecomas typically measure 5-10 cm in diameter. The cut surface is usually solid and yellow, but it can be focally white. Microscopically, sheets of uniform cells with oval to round nuclei and pale greyish-pink cytoplasm with ill defined borders are seen. The cytoplasm is rarely noticeably lipid rich. Mitoses are uncommon in tumours that have little or no nuclear atypia. Reticulin typically surrounds individual cells in thecomas.

Reticulin typically surrounds individual cells in thecomas. The majority of tumours are immunoreactive to inhibin, calretinin, and FOXL2. A strong inhibin staining favours the diagnosis of thecomas over fibromas.[31]

Luteinized thecoma associated with sclerosing peritonitis

They usually occur in premenopausal females and are bilateral. It is adistinct stromal tumour that is frequently associated with sclerosing peritonitis. Spindled cells are often negative for sex cord markers, whereas luteinized cells are positive.

Sclerosing stromal tumour

They mostly affect young females in their second to third decades of life and are unilateral. It is a benign stromal tumour made up of admixed rounded and spindled cells arranged in cellular nodules in a hypocellular, oedematous, or collagenous stroma. The tumour cells are vimentin positive, and they frequently stain for SMA, with the SMA stain concentrated in the plump cells in the perivascular regions of the tumour. [31]

Signet ring stromal tumour

These tumours are usually unilateral and occur in females aged 21 to 83. In a background fibromatous stroma, it is a benign stromal tumour with cells with signet-ring morphology but no intracytoplasmic mucin, glycogen, or lipid. Signet-ring cells express vimentin and smooth muscle actin and may show focal broad spectrum cytokeratin positivity but they are negative for EMA, inhibin and mucin stains.

Microcystic stromal tumour

It is a rare, benign ovarian tumour with a distinct microcystic appearance that is most likely of stromal origin. It is usually unilateral and appears at the age of 45. Microcysts, solid cellular zones, and collagenous stroma are the three components that vary in quantity. Microcysts typically predominate, with small rounded to oval cystic spaces in areas coalescing into larger irregular channels; intracytoplasmic vacuoles are also common. Collagenous stroma with hyaline plaques frequently intersects the solid cellular areas. The cells have a moderate amount of finely granular, lightly eosinophilic cytoplasm, round to oval or spindle-shaped nuclei, and small indistinct nucleoli. Bizzare nuclei are frequently found. Mitotic activity is minimal. Tumour cells are typically CD10 positive, whereas inhibin and calretinin are usually negative. Cytokeratins are occasionally found to be focally positive, whereas epithelial membrane antigen is negative. Nuclear immunoreactivity for WT1 and β-catenin has been observed.

Steroid cell tumour, NOS

These tumours are usually unilateral and appear around the age of 40. Macroscopically: These tumours have an average circumference of 8 cm.[31] On cut section these are solid and yellow, orange, red, brown, or black in colour. In cases of Leydig cell tumour, haemorrhage is more common. Microscopically: Tumour cells are arranged in a diffuse pattern, but they can also appear as nests and cords. Tumour cells are polygonal with abundant cytoplasm that ranges from eosinophilic (lipid-poor) to pale and vacuolated (lipid-rich), with the latter being much more common than in Leydig cell tumour. There may be varying amounts of intracytoplasmic lipochrome pigment present. The nuclei are usually round with a prominent central nucleolus; there is rarely significant nuclear atypia, which is usually accompanied by increased mitotic activity. Nearly one-third of steroid cell tumours, NOS exhibit malignant behaviour. Size > 7 cm, > 2 mitoses/10 HPF, necrosis, haemorrhage, and significant nuclear atypia are all predictors of malignancy. Immunohistochemistry: these tumours are positive for inhibin, calretinin, and steroidogenic factor-1. They are usually Melan-A positive[32] and FOXL2 negative. AFP is found to be positive in 50-90% of cases.

Leydig cell tumour

20% of steroid cell tumours are Leydig cell tumours. They usually occur at the age of 58 and are unilateral. Macroscopically: These tumours are typically small (2.4 cm on average) and have a solid cut section. They range in colour from red-brown, yellow to black. The majority form in the ovarian hilus, but they can also form rarely in the ovarian stroma ("non-hilar type"). Microscopically, these tumours are well circumscribed, with abundant eosinophilic, but occasionally pale, lipid-rich cytoplasm. Nuclei are typically round and bland, with prominent central nucleoli and nuclear pseudoinclusions. Usually lipochrome pigment is noted. Clustering of nuclei, resulting in eosinophilic nuclear-free zones, is a distinguishing feature. The presence of rare

cytoplasmic Reinke crystals (rod-shaped elongated eosinophilic inclusions) confirms the diagnosis. Mitoses are uncommon or non-existent. Fibrinoid necrosis of blood vessel walls is seen in some cases.

Immunohistochemistry: Sex cord-stromal markers such as inhibin, calretinin, and steroidogenic factor-1 are positive in Leydig cell tumours. They are usually Melan-A positive and AFP negative.

Fibrosarcoma

It is a malignant fibroblastic tumour. It usually affects postmenopausal females and is unilateral. These neoplasms are typically hypercellular, with long fascicles of spindle cells. The nuclei have moderate to severe atypia, and mitotic figures, which frequently include abnormal forms. In the absence of moderate to severe atypia, mitotic activity of 4 per 10 HPF in an ovarian cellular fibromatous neoplasm does not indicate a fibrosarcoma. Immunohistochemistry: These tumours are immunohistochemically positive for vimentin and, in some cases, SMA. These are cytokeratin and EMA negative.

Sex cord-stromal tumours - pure sex cord tumours

Adult granulosa cell tumour

Adult granulosa cell tumours appear at the age of 53 years. Postmenopausal bleeding is the most common presentation in older women, followed by menorrhagia, metrorrhagia, or amenorrhea in younger patients. Macroscopically: These are typically unilateral, with a mean size of 10 centimetres. They are usually solid and cystic, but they can also be solid or entirely cystic. The solid areas are typically soft and tan to yellow in colour. Microscopically, tumour cells frequently grow in cords and trabeculae, undulating ribbons, and nests (insular pattern). A microfollicular pattern in which granulosa cells surround small spaces containing eosinophilic secretions (Call-Exner bodies). Tumour cells typically have scant pale cytoplasm, but on rare occasions, the cytoplasm is abundant and eosinophilic (luteinized). The

nuclei are usually uniform, pale, and round to oval in shape. Nuclear grooves are a distinguishing feature, but they are not always visible in tumours. Atypia of the nucleus is usually absent. Mitotic activity varies.

Immunohistochemistry: Inhibin, calretinin, FOXL2, steroidogenic factor-1 (SF-1), WT1, and CD56 positivity is common in granulosa cell tumours.[33] They may be positive for broad-spectrum and low-molecular-weight keratins (8 and 18), but they are usually negative for CK7 and EMA. Smooth muscle actin, desmin, CD99 (membranous), and S-100 protein may be present.

Juvenile granulosa cell tumour

A specific type of granulosa cell tumour that primarily affects children and young adults. This variant is most common in the first three decades of life. Menorrhagia, abdominal or pelvic pain, distension, or a palpable mass are presenting symptoms. Macroscopically: The average size is 12 cm, and they are solid and cystic, though some are uniformly solid or cystic. The solid areas are yellow or tan in colour. Haemorrhage may be visible within cysts and solid foci. Microscopically: The tumour grows in a nodular or diffuse pattern. The cytoplasm of the cells lining the follicles and solid areas is typically eosinophilic, but occasionally pale amphophilic. With a few exceptions, the nuclei are round and lack grooves. Mitotic figures are common, and striking nuclear atypia is seen in 10-15% of tumours. The stroma is less visible and contains secretions that can be eosinophilic but are more commonly basophilic and can stain for mucin.

Immunohistochemistry: Inhibin, calretinin, SF-1, CD99, and CD56 are positive in these tumours.

Sertoli cell tumours

These tumours appear around the age of 30 and cause abdominal pain, swelling, and vaginal bleeding. Macroscopically: These are unilateral neoplasms that are on an average 8 cm in size. They are

usually solid, but they can also be solid and cystic or cystic. Solid areas are tan to yellow, with signs of haemorrhage and necrosis.

Microscopically: Majority of tumours have a tubular pattern, which can be hollow or solid. Trabecular, diffuse, alveolar, pseudopapillary, retiform, and spindled patterns can also be seen. The cytoplasm of cells typically ranges from pale and lipid-rich to eosinophilic. In most cases, nuclei are oval or round with a small nucleolus and are cytologically bland. The presence of a single Leydig cell within the tumour does not rule out Sertoli cell tumour as a diagnosis.

Immunohistochemistry: WT1, SF-1, cytokeratins, inhibin, calretinin, and CD99 are all found in the majority of tumours. Smooth muscle actin and S-100 are found in a small percentage of neoplasms, whereas EMA is negative.

Tumour of the sex cord with annular tubules

It is a rare sex cord-stromal tumour with a distinct pattern of simple and complex annular tubules. These can occur sporadically or in conjunction with Peutz-Jeghers syndrome (occurs at a younger age group). Macroscopically: The majority of tumours are solid, some are solid and cystic, and a few are uniformly cystic. On cut surface it is tan or yellow. The tumour is made up of individually dispersed or nodular aggregates of simple or complex annular tubules. Tubules typically lack lumens, and the nuclei of the lining cells are antipodal. The stroma is fibrous, and the tumour cell nests are surrounded by eosinophilic hyaline material that is continuous with the hyaline cores of the nests. Calcification is common in tumours associated with syndromes.

Immunohistochemistry: Typically, tumour cells express inhibin, calretinin, FOXL2, SF1, WT1, and CD56. Cytokeratins may be positive, but EMA is negative.

Mixed sex cord- stromal tumours

Sertoli-Leydig cell tumour

Tumours made up of varying proportions of Sertoli cells, Leydig cells, and, in the case of moderately and poorly differentiated neoplasms, primitive gonadal stroma and, occasionally, heterologous elements. Serum AFP levels may be elevated. Sertoli Leydig cell tumours occur in females aged 1 to 84, with a mean age of 25 years. Patients may complain of abdominal pain or ascites. Amenorrhoea, hirsutism, breast atrophy, clitoral hypertrophy, and hoarseness are effects of androgenic manifestations, whereas estrogenic manifestations include isosexual pseudoprecocity and menometrorrhagia. Macroscopically, these tumours are unilateral. Its size range from 2 to 35 cm. They can be solid, solid and cystic, or cystic. The solid areas are fleshy and can be pale yellow, pink, or grey. There may be areas of haemorrhage and necrosis. Microscopically, Sertoli cells are present in open or closed tubules in well-differentiated Sertoli-Leydig cell tumours and lack significant nuclear atypia or mitotic activity. Leydig cells are found in small clusters, cords, and singly in a delicate fibrous stroma. Hyalinization and ossification are uncommon.[34] An edematous stroma separates cellular lobules composed of darkly stained Sertoli cells, typically with scant cytoplasm and admixed in an unorganised fashion with Leydig cells, in tumours of moderate differentiation.

Immunohistochemistry: These are positivity for vimentin, keratin, inhibin, and calretinin, with varying degrees of expression in the sex cord and stromal areas. CD 56, SF-1, and WT-1 are all positive in Sertoli-Leydig cell tumours; 50% express CD 99, which does not stain the Leydig cell component. FOXL2 is expressed in at least 50% of Sertoli-Leydig cell tumours. FOXL2, WT1, and CD 99 staining is absent or minimal in Leydig cells in Sertoli-Leydig cell tumours, but MelanA expression is present.

Sex cord stromal tumours, NOS

Histological characteristics vary, but distinct features of a specific sex cord-stromal tumour are uncommon.

Germ cell tumours

Dysgerminoma

It is a primitive germ cell tumour with no discernible differentiation pattern. Majority of children and young females are affected. Patients presents clinically with complaints of abdominal distension, an abdominal mass, or abdominal pain. Serum lactic dehydrogenase (LDH) levels are frequently elevated, and human chorionic gonadotropin levels may also be elevated (HCG). They are mostly unilateral. Macroscopically: These tumours are typically larger than 10 cm in diameter and have a solid, fleshy tan or white cut surface. There may be haemorrhage, necrosis, or foci of cystic degeneration. Microscopically: It is made up of polygonal sheets or nests with abundant granular eosinophilic or clear cytoplasm and distinct cell membranes. Tumour cells have angulated nuclei that are uniformly medium in size, with vesicular chromatin and prominent nucleoli. Numerous mitotic figures are seen. The tumour is intersected by fibrous septa containing lymphocytes (mostly T-cells).[35]

Immunohistochemistry: The tumour cells are immunoreactive for cytoplasmic and membranous placental alkaline phosphatase (PLAP) and membranous CD117(c-KIT). The stem cell/primitive germ cell nuclear transcription factors OCT-4, NANOG, and SALL4 show diffuse positive nuclear staining.

Yolk sac tumour

These are primitive germ cell tumours. Macroscopically, t hese tumours are well encapsulated, large, and soft. The cut surface is grey-yellow, with necrosis, haemorrhage, and cystic degeneration. Microscopically, the tumour can be seen in more than two patterns, the most common of which is the reticular pattern. Stroma is myxoid, loose, and

hypocellular. Long arching cords (festoon pattern) and papillary growth are two other patterns. Schiller duval bodies can also be noted.

Immunohistochemistry: These tumours express AFP (often focally), glypican-3 (stronger than AFP but less specific), and SALL4. Yolk sac tumour, on the other hand, is negative for OCT4, SOX2, D2-40, and CD30.

Embryonal carcinoma

Embryonal carcinoma is almost always found in children and young women. The serum Beta-HCG level is frequently elevated. Macroscopically, these are large, solid tumours with a 15 cm average diameter. The cut surface is soft and fleshy, with cysts of varying sizes. The tumour is tan or grey in colour, with prominent areas of haemorrhage and necrosis. Microscopically, the tumour grows in sheets or nests with focal glandular differentiation. Tumour cells are polygonal having vesicular nuclei with coarse, basophilic chromatin and one or two prominent nucleoli. The cell membranes are well defined, and the cytoplasm is abundant, amphophilic most of the time but occasionally focally clear. There are numerous mitotic figures and apoptotic bodies. Synytiotrophoblast cells are also seen.

Immunohistochemistry: Cytokeratin (AE1/AE3), CD30, OCT4, SALL4, and glypican 3 are commonly positive in tumour cells. SOX2 has varying degrees of positivity. Epithelial membrane antigen is negative. If present, syncytiotrophoblasts are cytokeratin and HCG positive.

Non- gestational choriocarcinoma

It is a germ cell-derived malignant neoplasm composed of cytotrophoblast and syncytiotrophoblast cells. It is common in young females and can look like an ectopic pregnancy. Serum beta- hCG levels range from hundreds to thousands of mIU/ml. [36] hCG and inhibin stain positive in the cytoplasm of syncytiotrophoblastic cells. Trophoblastic cells express CD10, EMA, and cytokeratins.

Mature teratoma

It is a tumour that is entirely made up of mature tissues derived from two or three germ layers (ectoderm, mesoderm and endoderm). Tumours are typically cystic (mature cystic teratoma), but they are rarely solid (mature solid teratoma). It usually occurs during reproductive age groups. Unless malignant transformation occurs, these tumours are benign. Immunohistochemistry has a limited role in diagnosing a teratoma.

Immature teratoma

It is the second most common malignant germ cell tumour of the ovary. It is usually unilateral, large, solid, fleshy, and grey-tan in colour, with cysts, haemorrhage, and necrosis. It usually occurs during the first three decades of life. This tumour contains varying amounts of immature (typically primitive/embryonal neuroectodermal) tissues, including embryoid bodies in its most primitive forms.

Immunohistochemistry: SALL4 is expressed in the intestinal and immature neural elements.[37] In the neuroepithelium, SOX2 and glypican 3 are positive, and AFP may stain immature gastrointestinal-type glands.

Monodermal teratomas and somatic tumours that develop from a dermoid cyst

Struma ovarii

A mature monodermal teratoma composed entirely or primarily of thyroid tissue. It can be both benign and malignant. It occurs in women of reproductive age. Thyroglobulin and TTF1 are immunohistochemically expressed in tumour cells.

Carcinoid

The most common type of primary ovarian carcinoid tumour is an insular carcinoid. Carcinoids frequently express one or more neuroendocrine markers and often stain for CDX2.

Neuroectodermal- type tumour

These are rare tumours with morphology and differentiation similar to neuroectodermal tumours of the central nervous system. These are composed of neuroectodermal tissue. These tumours frequently express CD99. Primary ovarian ependymomas are more likely to express cytokeratins, as well as ER and PR.

Sebaceous tumours

Neoplasms that resemble different types of cutaneous sebaceous gland tumours (sebaceous adenoma, basal cell carcinoma with sebaceous differentiation, sebaceous carcinoma) and can develop within a dermoid cyst. The most distinguishing feature of these tumours is the large number of mature, foamy or bubbly sebaceous cells that stain with oil red-O.

Squamous cell carcinoma

The most common type of squamous cell carcinoma is one that develops from malignant transformation within a dermoid cyst. Cytokeratins are frequently found in these tumours.

Others

Adenocarcinoma is the second most common type of cancer that develops in dermoid cysts.

Mixed germ cell tumours

It affects young women. Serum levels of LDH, AFP, and beta-hCG are usually elevated. It is made up of two or more malignant, primitive, germ cell components. Dygerminoma and yolk sac tumour are the most common admixtures.

Immunohistochemistry: OCT4, CD30, glypican 3, and GDF3 are useful markers for characterising tumour components.

Germ cell - sex cord stromal tumours

Gonadoblastoma

It is an "in situ" form of malignant germ cell tumour composed of immature sex cord cells and germ cells. It is more common in phenotypic females with gonadal dysgenesis and an abnormal karyotype, but it can also occur in seemingly normal females with a 46 XX karyotype. It occurs mostly in young females.

Immunohistochemistry: Placental alkaline phosphatase, CD117 (c-Kit), OCT-4, NANOG, and SALL4 are all positive in germ cells. The sex cord-type cells typically stain with inhibin, calretinin, WT-1, and FOXL2, but not SOX9.

Mixed germ cell - sex cord stromal tumour, unclassified

A neoplasm made up of germ cells and sex cord elements that occurs in genetically and phenotypically normal females but lacks the distinctive appearance of a gonadoblastoma.

Immunohistochemistry: The sex cord elements are inhibin immunoreactive. The germ cells are immunoreactive for PLAP, OCT4, and c-Kit protein and resemble dysgerminoma cells.

Mesenchymal tumours

Leiomyomas

It is a soft tissue tumour that is benign in nature. On gross examination, it appears to be a well-circumscribed, unencapsulated tumour. On cut section is white and whorled. Microscopically, these tumours are arranged in intersecting fascicles. The cytoplasm of the cells is eosinophilic, with cigar-shaped nuclei and small nucleoli. There are also hyalinised areas.

Immunohistochemistry

Leiomyomas express desmin and h-caldesmon, smooth muscle actin, smooth muscle myosin, ER, PR, and WT1.

Smooth muscle tumour of uncertain malignant potential

It is a smooth muscle tumour with characteristics that preclude an unequivocal diagnosis of leiomyosarcoma, do not meet the criteria for leiomyoma or its variants, and raise concern that the neoplasm may be malignant. The three histological features necrosis, mitosis, and nuclear atypia are used to make the diagnosis.

These tumours are immunohistochemically positive for p16 and p53.

Leiomyosarcoma

It is a mesenchymal tumour that is malignant. Microscopically, the tumour cells are cytologically high-grade with eosinophilic cytoplasm that form interlacing disorganised fascicles. Mitosis is present in these tumours, and atypical mitosis is common.

Most tumours show positive staining for desmin, h-caldesmon, and smooth muscle actin. These tumours strong positive for p16 and p53.

Low grade endometrioid stromal sarcoma

It is similar to low grade uterine endometrial stromal sarcoma. LGESS is composed of sheets of small, closely packed cells that resemble the stromal cells of proliferative endometrium, with scanty cytoplasm, round to oval nuclei, and small blood vessels that resemble the spiral arterioles of late secretory endometrium. Storiform fibrosis, a "starburst" pattern of hyaline plaques, foamy cell change, sex cord-like differentiation, and myxoid change are also observed.

LGESS shows diffuse strong positivity for CD10 immunohistochemistry, but this is not specific for an endometrioid stromal tumour.[38] These tumour cells are positive for SMA and, on occasion, desmin, but negative for h-caldesmon. These tumours are typically ER and PR positive.

High grade endometrioid stromal sarcoma

A mesenchymal tumour with endometrial stromal differentiation and brisk mitotic activity, with high-grade cytologic atypia. The

resemblance to proliferative endometrial stromal cells in the high-grade regions of the tumour is lost.

Immunohistochemistry reveals strong and diffuse expression of cyclin D1 and the absence of CD10 in epithelioid rounded cells, whereas CD10 is present in the cytologically bland spindle fibromyxoid component. Spindled cells express ER and PR.

Ovarian myoxma

A mesenchymal neoplasm composed of bland spindle-shaped cells embedded in abundant myxoid. It is a rare benign neoplasm. Smooth muscle actin is positive the tumour cells, but desmin, S100, cytokeratins, and epithelial membrane antigen are negative.

Mixed epithelial and mesenchymal tumours

Adenosarcoma

It is a rare biphasic tumour composed of malignant mesenchymal and benign to atypical epithelial component. This tumour is unilateral and develops during the fifth decade of life. Stroma has a biphasic arrangement of glands with mild to moderate cytological atypia. The glands are distributed uniformly and are frequently lined by endometrioid-type epithelium, which is benign or atypical but not malignant. Papillary to polypoid frondsof stroma frequently project into cystic glands or project from the tumour's surface. Stromal overgrowth can also show rhabdomyomatous differentiation, with the cells expressing desmin and myogenin. The stromal component is typically positive for CD10, ER, and PR.

Carcinosarcoma

A biphasic neoplasm with malignant epithelial and mesenchymal elements. These are made up of high-grade carcinoma and sarcoma components. The carcinomatous component is usually a high-grade serous carcinoma, but other histological types can occur.[39] Sarcomas can be rhabdomyosarcoma, chondrosarcoma, osteosarcoma,

liposarcoma, or angiosarcoma. Desmin, myogenin, and myoD1 for rhabdomyosarcoma and S100 for chondrosarcoma can confirm the presence of heterologous components.

Metastasis

Metastases to the ovary are common and mostly epithelial in nature. The most common primary tumours that metastasize to the ovary are those that originate in the large intestine, stomach, appendix, and breast, female genital tract, including the endometrium and cervix, pancreas, and other locations throughout the body. Immunohistochemistry markers are commonly used to differentiate between primary ovarian tumours and metastasis. CDX2, SATB2, MUCSs, GATA3, ER, PR, vimentin, TTF-1, PAX8, CK20, and other markers are used.

Miscellaneous tumours

Miscellaneous tumours include rete ovarii, wolffian tumours, small cell carcinomas- hypocalcaemic type, wilms tumour, small cell carcinomas-pulmonary type, paraganglioma, and solid pseudopapillary tumours.

Role of immunohistochemistry in ovarian neoplasms

Some of the commonly used immunohistochemical markers for ovarian neoplasms are:

Epithelial Ovarian Neoplasm

Cytokeratin profile- Nearly all of the primary epithelial tumours of the ovary are CK7 positive so lack of staining for CK7 suggests the possibility of metastasis. Mucinous tumours stains for CK20 which are usually negative in other primary epithelial tumours.

CEA - In ovarian cancers, CEA is not often positive except for mucinous adenocarcinoma, which is typically CEA positive.

EMA- Diffuse positive staining for EMA suggests an epithelial tumour, either primary or metastatic, mimicking a sex cord–stromal tumour. Sex cord–stromal tumours are almost always EMA negative.

CA125- Staining of the cell membranes with CA 125 is typically positive in serous carcinoma.

WT1- Expression is seen in serous carcinoma of the ovary, fallopian tube, and peritoneum but expression in serous carcinoma of the endometrium tends to be limited.

β-catenin- Among the epithelial tumours, endometrioid neoplasms are most likely to show nuclearstainingfor β-catenin and rarely seen in serous carcinomas.

ER, PR, Vimentin-ER and PR expression is moderate to strong in endometrioid carcinomas, but are rarely expressed in clear-cell carcinomas. Serous carcinomas express ER andless commonly PR. Vimentin is mostly expressed in endometrioid carcinomas.

GATA3-It has emerged as a useful marker for Brenner tumours, as most show diffuse positive staining with this marker.

p53- A strong positive nuclear staining for p53 is found in serous carcinomas. Low grade serous carcinoma, which appears to evolve via a different pathway than high-grade serous carcinoma and is significantly less likely and of lesser intensity than high-grade serous carcinoma to express p53.

PAX8- It is extremely useful in confirming mullerian origin of the tumour.

NapsinA-It is highly expressed in clear cell carcinomas of the ovary.

Sex Cord-Stromal Tumours

Inhibin, calretinin, SF1, FOXL2- It is a sensitive and relatively specific marker of sex cord–stromal tumours of the ovary. Inhibin, calretinin, and SF-1, FOXL2 together these markers can be used in an IHC panel for positive identification of sex cord–stromal tumours.

Germ Cell Tumours

PLAP- Placental alkaline phosphatase (PLAP) is a marker for malignant GCTs, especially dysgerminoma and embryonal carcinoma.

AFP- Alpha-fetoprotein (AFP) is an oncofetal glycoprotein expressed in yolk sac tumour and its variants, including hepatoid and endometrioid yolk sac tumour. Although focal expression can be seen in embryonal carcinomas and in hepatic or enteric tissues in teratomas.

CD117 - CD117 does not stain embryonal carcinoma and is thus a more specific marker of dysgerminoma than PLAP.

Glypican3- It is highly expressed by yolk sac tumours.

hCG- Primary ovarian tumours that contain syncytiotrophoblastic cells, including choriocarcinoma and some dysgerminomas and embryonal carcinomas, express hCG.

SALL4- It is a highly sensitive marker for yolk sac tumour, dysgerminoma, embryonal carcinomas, choriocarcinoma, and teratoma.

OCT4– Germ cell tumours such as dysgerminoma and embryonal carcinoma are nuclear positive for OCT4. Other types of Germ cell tumours are negative. OCT4 has proven to be an excellent immunostain as its staining is strong and diffuse.[13]

In 2000, a study was conducted by Ordonez NG et al[40] considering the microscopic resemblance to transitional epithelium (urothelium), Brenner tumour (BT) of the ovary which is commonly described as a transitional cell neoplasm. The immunophenotype of 8 benign BTs were evaluated together with that of 12 TCCs of the bladder using antibodies to thrombomodulin (TM), cytokeratin 20, cytokeratin 7, and carcinoembryonic antigen (CEA), all of which have been shown to react with TCCs of urothelial origin. They concluded that all 8 benign BTs exhibited strong diffuse reactivity for cytokeratin 7(100%), but none stained for cytokeratin 20 (0%). 4 of the 8 showed focal positivity

for CEA. Reactivity for TM occurred in the endothelium of the blood vessels, but in all of the cases the tumour cells were negative (0%). All 12 TCCs of the bladder displayed immunoreactivity for TM, and the staining was especially visible along the cell membranes. Cytoplasmic reactivity for cytokeratins 20 and 7 was demonstrated in all of the tumours (100%). 7 of the 12 also exhibited CEA positivity (58%). The special studies thus reveal differences between BT and TCC that are not apparent by routine light microscopy.

In 2005, Longani S et al[41] conducted a study to distinguish primary ovarian carcinomas from metastatic colorectal cancers. In their study they tried to distinguished primary ovarian carcinoma, particularly endometrioid and mucinous subtypes, from metastatic colorectal carcinoma to the ovary which is often difficult on histologic examination alone. They used three immunohistochemical markers CDX2, a homeobox gene encoding an intestine-specific transcription factor; a-methylacyl-CoA racemase (AMACR/P504S) and b-catenin, an adenomatous polyposis coli (APC) mutation product which have been reported to have specific and sensitive expression in colorectal carcinomas. They evaluated a panel consisting of antibodies to CDX2, b-catenin and P504S in 23 primary ovarian adenocarcinomas (13 mucinous and 10 endometrioid) and compared the findings to 22 metastatic colorectal adenocarcinomas (seven mucinous and 15 nonmucinous tumours with endometrioid-like morphology (referred to as pseudo-endometrioid) to the ovary stained with the same panel. They found that twenty (91%) metastatic tumours expressed at least two markers and seven (32%) expressed all three. In contrast, only three (13%) primary ovarian tumours expressed at least two markers and none expressed all three. Strong and diffuse (440%) expression for CDX2 was noted in 21 (95%) metastatic tumours and five (22%) primary ovarian tumours (three mucinous, two endometrioid). P504S was similarly expressed in seven (32%) metastatic and none of the primary ovarian carcinomas. Nuclear expression of b-catenin was noted in 13 (59%) metastatic tumours and in eight cases (36%), it was

diffuse and strong. In contrast, four (19%) primary tumours showed nuclear expression of this protein with only one (5%) case expressing it in a diffuse pattern. Immunohistochemical expression of gene products and enzymes of colorectal carcinogenesis in some primary ovarian carcinomas suggest that the morphologic similarities between colorectal and mucinous/endometrioid carcinoma of the ovary extends to the genetic level, although differences in the level of expression exist between these tumours. Diffuse expression of all three markers (CDX2, b-catenin and P504S) in a tumour in the ovary was found to be virtually diagnostic of metastasis from a colorectal primary in their study.

In 2006, a study was conducted by Netinatsunthorn W et al[42], regarding WT1 gene expression as a prognostic marker in advanced serous epithelial ovarian carcinoma: an immunohistochemical study. WT1 is a tumour suppressor gene responsible for Wilms' tumour. WT1 reactivity is limited to ovarian serous carcinomas. The aim of their study was to determine the survival and recurrence-free survival of women with advanced serous epithelial ovarian carcinoma in relation to WT1 gene expression. The study accrued women over an 18-year period, from 1987–2004. During the study period, 163 patients were diagnosed with advanced serous epithelial ovarian carcinoma and had undergone complete post-operative chemotherapy, but the final study group comprised 99 patients. The records of these women were reviewed and the paraffin-embedded tissue of these women stained with WT1 immunostaining. Survival analysis was performed using Kaplan-Meier and Cox regression methods. In results 50 patients showed WT1 staining and 49 did not. They concluded that five-year survival of nonstaining and staining groups were 39.4% and 10.7% ($p < 0.00005$); five-year recurrence-free survival of these groups were 29.8% and ≤ 7.5% ($p < 0.00005$), respectively. For survival the HR of WT1 staining, adjusted for residual tumour and chemotherapy response, was 1.98 (95% CI 1.28–3.79), and for recurrence-free survival the HR was 3.36 (95% CI 1.60–7.03). The HR for recurrence-free survival was not confounded by any other variables. Their study

suggested that expression of WT1 gene may be indicative of an unfavourable prognosis in patients with advanced serous epithelial ovarian carcinoma.

The main neoplasms in the differential diagnosis for primary ovarian tumours with a tubule-rich pattern are pure Sertoli cell tumour, endometrioid tumours (including borderline tumour, well-differentiated carcinoma, and the sertoliform variant of endometrioid carcinoma), and carcinoid tumour. In 2007, Zhao C et al[43], did a study on 160 cases using immunohistochemistry to distinguish ovarian Sertoli cell tumours from endometrioid and carcinoid tumours. In their study they stated that traditional immunohistochemical markers [pan-cytokeratin (pan-CK), low molecular weight cytokeratin (CK8/18), epithelial membrane antigen (EMA), inhibin, calretinin, CD99, chromogranin, and synaptophysin] can occasionally have diagnostic limitations, the goal of their study was to determine whether or not any alternative markers [cytokeratin 7 (CK7), estrogen receptor (ER), progesterone receptor (PR), CD10, and CD56] have better diagnostic utility when compared with traditional markers for this differential diagnosis. For the results, immunohistochemical stains for alternative, as well as traditional, markers were performed on the following primary ovarian tumours: pure Sertoli cell tumour (n = 40), endometrioid borderline tumour (n = 38), sertoliform endometrioid carcinoma (n = 13), well-differentiated endometrioid carcinoma (n = 27), and carcinoid tumour (n = 42). Extent and intensity of immunostaining were semiquantitatively scored. In addition, immunohistochemical composite scores (ICSs) in positive cases were calculated on the basis of the combination of extent and intensity scores. They concluded that in their study Cytokeratin 7 (CK7) was positive in 97% of endometrioid tumours, 13% of Sertoli cell tumours, and 24% of carcinoid tumours. The differences in the mean ICSs for endometrioid tumours versus Sertoli cell tumour or carcinoid tumour were statistically significant (P values ranging from <0.001 to 0.018). ER and PR were positive in 87% and 86% of endometrioid tumours, 8% and 13% of Sertoli cell tumours, and 2% each of carcinoid

tumours, respectively. The differences in the mean ICSs for endometrioid tumours versus Sertoli cell tumour were statistically significant (P values ranging from <0.001 to 0.012). Among the epithelial markers, EMA seemed to be the most discriminatory but only slightly better than CK7, ER, or PR. Pan-CK and CK8/18 were not helpful. CD10 showed overlapping patterns of expression in all categories of tumours. Among the sex cord markers, CD10 was markedly less useful than inhibin or calretinin; CD99 was not discriminatory. CD56 showed overlapping patterns of expression in allcategories of tumours. Among the neuroendocrine markers, CD56 was less useful than chromogranin or synaptophysin. They discussed that when traditional immunohistochemical markers are problematic for the differential diagnosis of ovarian Sertoli cell tumour versus endometrioid tumours versus carcinoid tumour, adding CK7, ER, and/or PR to a panel of markers can be helpful. Endometrioid tumours more frequently express CK7, ER, and PR and show a greater extent of immunostaining in contrast to Sertoli cell tumour and carcinoid tumour. Compared with traditional epithelial markers, CK7, ER, and PR are nearly as advantageous as EMA. Inhibin is the most discriminatory sex cord marker, and CD10 is not helpful in the differential diagnosis. Chromogranin and synaptophysin are excellent discriminatory markers for carcinoid tumour, and CD56 is neither sufficiently sensitive nor specific enough for this differential diagnosis to warrant its use in routine practice.

In 2009, Cao D et al[44], conducted a study on 261 cases to distinguish yolk sac tumour from clear cell carcinoma. Ovarian primitive germ cell tumours (GCTs) are uncommon tumours and sometimes pose diagnostic challenges. Among them, yolk sac tumour (YST) poses the greatest diagnostic difficulty and can be mistaken for clear cell carcinoma (CCC). In their study on immunohistochemistry, they investigated a novel marker SALL4 in 98 GCTs (29 YSTs, 18 dysgerminomas, 6 gonadoblastomas, 6 embryonal carcinomas, 15 immature and 12 mature teratomas, 7 carcinoid tumours, 3 strumal

carcinoids, and 2 struma ovarii) with particular interest of exploring SALL4 to distinguish YST from CCC. One hundred sixty-three non-GCTs including 45 CCCs were also stained. In inference, SALL4 was strongly positive in more than 90% tumour cells in all YSTs, dysgerminomas, gonadoblastomas, and embryonal carcinomas. Variable SALL4 staining was seen in 11 of 15 immature teratomas. All other GCTs included in the study were negative for SALL4. Except 3 CCCs with focal SALL4 staining (<15% tumour cells), SALL4 was negative in the remaining 160 non-GCTs. They also compared SALL4 with AFP, glypican-3, CK7, and EMA in all YSTs and CCCs. AFP and glypican-3 were positive in 24 (83%) and 20 (69%) YSTs, respectively, whereas 16 (35%) and 13(28%) CCCs showed positive AFP and glypican-3 staining, respectively. Three (10%) and 4 (14%) YSTs showed focal (<2% tumour cells) CK7 and EMA staining, respectively. CK7 and EMA were positive in all 45 CCCs but 3 (7%) and 1 (2%) cases showed staining in less than 30% tumour cells, respectively. They concluded that SALL4 is a novel sensitive and specific marker for ovarian primitive GCTs. SALL4 is particularly useful in distinguishing YST from CCC and better than AFP, glypican-3, CK7, and EMA.

In 2010, Shin JH et al[45] conducted a study of 63 cases to distinguishmetastatic colorectal carcinoma (MCAOs) involving ovary from primary ovarian mucinous adenocarcinoma (POMAs) using immunohistochemistry markers. They evaluated the immunohistochemical (IHC) expression of cytokeratin 7 (CK7), cytokeratin 20 (CK20), CDX2, CEA, MUC2, MUC5AC and alpha-methylacyl-CoA racemase (AMACR) in 22 POMAs and 41 metastatic colorectal adenocarcinomas (MCAOs) involving ovaries. The results of the study were MCAOs, in contrast with POMAs, were almost always negative for MUC5 (97.6%), often negative for CK7 (82.9%), focal or diffuse positive for CDX2 (73.2%), diffuse positive for CK20 (65.9%), focal or diffuse positive for MUC2 (51.2%), diffuse positive for CEA (41.5%) and negative for AMACR (41.5%). They considered CK7 (-), CK20 (diffuse +), CDX2 (+) and MUC2 (+) to be colonic markers and

regarded cases with expression of more than two colonic markers as MCAO, those with no expression of colonic markers as POMA and those with expression of one colonic marker as indeterminate. Using CK7/CK20/CDX2/MUC2, 82.5% of the cases were correctly classified, 6.3% were misclassified and 6.3% were indeterminate. They concluded that CK7, CK20, CDX2 and MUC2 IHC staining is a useful adjunctive diagnostic tool to differentiate MCAOs from POMAs, in addition to clinical history and gross and microscopic findings.

In 2012, a study was conducted by Giurgea LN et al[46] regarding borderline epithelial tumours of the ovary. The aim of the study was to assess p53 and Ki67 immunohistochemical expression in 52 epithelial ovarian tumours, correlating with clinicopathological factors, and comparison between results in benign, borderline, and malignant tumours. In their study total number of 125 patients diagnosed with epithelial ovarian neoplasms in the period 2002–2010, 52 operated patients were selected, with serous and mucinous tumours. There were 26 (50%) malignant cases, 15 (28.8%) borderline and 11 (21.15%) benign. Results of the study were, p53 immunoreactions were positive in 41.66% of malignant serous tumours, most of them (90%) high-grade carcinomas; 6.66% of borderline and none of benign tumours were positive. Ki67 was positive in 61.53% of malignant cases, with higher percent in advanced clinical stages. Ki67 immunoreactions were also positive in borderline and benign tumours, with lower percent, 13.3% respectively 9.09%. In the conclusion of the study a similar frequency of immunostaining in borderline tumours and low-grade invasive serous carcinomas in contrast to the significantly higher frequency of p53 mutations in high grade serous carcinomas were found. Also an inference was made that the proliferative activity as assessed by Ki67 staining does not explain any possible relationship of serous borderline tumours to epithelial ovarian cancer.

In 2013, a study was conducted by Kriplani D et al[47], to differentiate primary epithelial ovarian tumours and metastatic tumours in the ovary. During their study period of 2 years they received 95 specimens and biopsies of primary ovarian neoplasms and neoplasms metastatic to the ovary. Of these 30 cases were of the primary surface epithelial neoplasms and 7 of metastatic tumours. The most common tumours metastasizing to the ovary originated from the gastrointestinal tract followed by the endometrium. They used a panel of six markers including cytokeratin-7 (CK7), CK20, carcinoembryonic antigen (CEA), cancer antigen 125 (CA125), estrogen receptor (ER) and Wilms' tumour 1 (WT1) to help classify various surface epithelial tumours as well as to differentiate them from tumours metastatic to the ovary. Three of four metastatic colorectal adenocarcinomas were negative for CK7 and CA125(75%). Three showed diffuse and strong positivity for CEA (75%). All were positive for CK20 (100%) and none reacted with ER and WT1 (0%). CK7, CK20 and CEA (100%) all showed a cytoplasmic pattern of staining. All serous ovarian and endometrial adenocarcinomas were positive for CK7 (100%) and none showed reactivity with CK20, CEA and WT1. CA125 positivity was seen in two endometrial adenocarcinomas and ER was positive in one. They concluded that CK7 is the most helpful marker to differentiate primary ovarian carcinoma from metastatic colorectal carcinoma of the ovary. Nearly, 96% of ovarian adenocarcinomas were positive for CK7 in contrast to metastatic colorectal, which showed only 25% positivity.

In 2016, a study was conducted by Cole AJ et al[48], which assessed mutant p53 in high grade serous carcinomas using immunohistochemistry. The study was done on 88 tumour specimensEighty-two percent (59/72) of HGSOCs were at an advanced stage, classified as Stage III or IV. A mutation in *TP53* was identified in 94% (68/72) of HGSOC. Four HGSOC were reported to be wild-type for *TP53* underwent second review of archived tissue by an experienced pathologist [AJG] and remained classified as HGSOC. An additional 4 samples contained clear cell components and were

excluded from this study. The 4 low-grade serous ovarian cancer (LGSOC) samples contained wild-type *TP53*. They concluded that p53 IHC may be used with care as a surrogate marker of *TP53* mutation by designating specimens demonstrating 'Intermediate' p53 staining as most likely p53 wild-type.

In 2018, Rekhi B et al[49] conducted a study on Napsin A as a sensitive and specific marker for clear cell carcinomas of ovary. Clear cell carcinoma (CCC) of the ovary is an uncommon, but an aggressive epithelial ovarian cancer (EOC), which has overlapping histopathologic features with other ovarian tumours. Lately, Napsin A has been identified as its useful diagnostic immunohistochemical (IHC) marker. Fifty-eight prospectively diagnosed ovarian CCCs, 53 high-grade serous carcinomas (HGSCs), 16 endometrioid adenocarcinomas (EMACs), 6 mixed carcinomas, containing components of CCC and EMAC, 7 metastatic mucinous adenocarcinomas and 6 ovarian yolk sac tumours (YSTs) were tested for Napsin A immunostaining. 50 ovarian CCCs, 50 HGSCs, 7 ovarian EMACs and 5 mixed carcinomas were tested for WT1 immunostaining. Napsin A was positively expressed in all 58 (100%) CCCs; was focally positive in 1 of 6 YSTs; in 1/16 EMACs and in 6 cases of mixed carcinomas, while it was negative in all 53 HGSCs and in 7 metastatic mucinous adenocarcinomas. Other IHC markers expressed in cases of CCC ovary were CK7 (31/31) (100%), WT1 (0/50), p53 (20/26, 'wild type'), ER (4/31, focal) (12.9%), PAX8 (14/14) (100%), glypican-3 (4/10, focal) (44.4%), p16INK4 (5/5, focal) and CK20 (0/5). Various IHC markers expressed in HGSCs were WT1 (48/50) (96%), p53 (31/31, mostly 'mutation type'), CK7 (9/9) (100%) ER (13/16, variable) (81.2%) and PAX8 (14/14) (100%). IHC markers expressed in EMACs were ER (15/16) (93.7%), CK7 (2/2) (100%) and WT1 (0/7). IHC markers expressed in mixed carcinomas were CK7 (2/2) (100%), WT1 (0/2), focal Napsin A (6/6) and focal ER (5/6). The sensitivity and specificity of Napsin A for the diagnosis of CCC ovary was 100% and 90.9%, respectively. The sensitivity and specificity of WT1 for diagnosis of

HGSC ovary was found to be 96% and 100%, respectively. Napsin A and WT1 are highly sensitive and specific IHC markers for diagnosing ovarian CCCs and HGSCs, respectively, and in differentiating these tumours from their mimics. Napsin A is useful in identification of component of CCC in certain EMACs.[49]

In, 2018 an article was published by Kutasovic JR et al[50], in which authors studied about breast cancer metastasis to gynaecological organs and the pattern of tumour spread. They explored clinico-pathological and molecular features of these metastases to better understand whether this pattern of dissemination is organotropic or aconsequence of wider metastatic dissemination. Primary and metastatic tumours from 54 breast cancer patients with gynaecological metastases were analysed using immunohistochemistry, DNA copy-number profiling, and targeted sequencing of 386 cancer-related genes. The median age of primary tumour diagnosis amongst patients with gynaecological metastases was significantly younger compared to a general breast cancer population (46.5 versus 60 years; $p < 0.0001$). Median age at metastatic diagnosis was 54.4, time to progression was 4.8 years (range 0-20 years), and survival following a diagnosis of metastasis was 1.95 years (range 0-18 years). Patients had an average of five involved sites (most frequently ovary, fallopian tube, omentum/peritoneum), with fewer instances of spread to the lungs, liver, or brain. Invasive lobular histology and luminal A-like phenotype were over-represented in this group (42.8 and 87.5%, respectively) and most patients had involved axillary lymph nodes ($p < 0.001$). Primary tumours frequently co-expressed estrogen receptor cofactors (GATA3, FOXA1) and harboured amplifications at 8p12, 8q24, and 11q13. In terms of phenotype conversion, estrogen receptor status was generally maintained in metastases, FOXA1 increased, and expression of progesterone receptor, androgen receptor, and GATA3 decreased. ESR1 and novel AR mutations were identified. Metastasis to gynaecological organs is a complication frequently affecting young women with invasive lobular carcinoma and luminal A-like breast

cancer, and hence may be driven by sustained hormonal signalling. Molecular analyses reveal a spectrum of factors that could contribute to de novo or acquired resistance to therapy and disease progression.

Clear cell carcinomas (CCC) differ from other types of ovarian and endometrial carcinomas in biology, behavior and response to chemotherapy. Histopathologic diagnosis may be challenging in some situations which necessitates immunohistochemistary (IHC) assessment. In 2020, Nili F et al[51] conducted in which they investigated the diagnostic utility of NapsinA in diagnosis of ovarian and endometrial CCCs. Ovarian and endometrial CCC samples from 2013 to 2018 in 3 general and women's hospital in Tehran were re-evaluated by 2 expert pathologists. Forty- two samples were included as cases and 42 non-clear cell carcinomas (Non-CCC) of ovary and endometrium were selected as control group. Based on IHC study tumours with sum intensity and percentage score ≥2 (at least 1+ staining in more than 1% of tumour cells) were considered positive. The results of the study were as stated that the prevalence of endometrial and ovarian CCC in the case group were 15 and 27 respectively. The tumours in the control group included 22 cases of endometrioid, 2 high grade papillary serous carcinoma (HGSC) of endometrium, 6 endometrioid and 12 HGSC of ovary. NapsinA positivity was observed in 35 (83%) of CCCs while 7 (17%) samples including 3 out of 15 endometrial and 4 out of 27 ovarian CCCs were NapsinA negative. No positive reaction was seen in control group. The overall accuracy, specificity and sensitivity of NapsinA for diagnosis of ovarian and endometrial CCCs were 83%, 100% and 83%, respectively. Sensitivity for ovarian and endometrial CCCs was 85% and 80%, orderly. It was concluded that NapsinA is an accurate and reliable marker for distinction of CCCs from nonCCCs in ovary and endometrium.

Ovarian cancers remain the most lethal of all gynecological malignancies despite major developments in their treatment. In 2020 Amanullah NA etal[52] conducted a study to understand the rate of

expression and staining patterns of p53 in various histological types and grades of epithelial ovarian tumours (EOT). During their study 60 EOTs were received in a tertiary care center and were studied for gross, microscopy, and p53 immunohistochemistry (IHC) expression patterns. Parameters such as age, laterality of tumour, ascites, and capsule rupture, and tumour size, stage at presentation, metastasis, tumour grade, and number of mitosis were correlated. Results of the 60 cases studied were as followed, out of 60 cases studied 23 (38.3%) were malignant. Serous carcinomas were the largest group with 17 cases (74%) followed by mucinous with 4 cases (17%) and 2 clear cell carcinomas (9%). All benign and borderline EOT were p53 negative. 65.2% of the malignancies were p53 positive and all of them were serous malignancies. 15 out of 16 high-grade serous carcinomas were p53 positive (94%), while one case was negative (6%). Ten cases (63%) showed intense diffuse positivity of more than 60% of the nucleus, while 5 cases (31%) showed aberrant null staining <5% staining of the nucleus. All mucinous, clear cell carcinomas and the only low-grade serous carcinoma in the study were p53 negative. P53 staining had positive correlations with variables like capsule rupture, ascites, laterality, and CA 125. Conclusion of the study highlights the different rates of expression and staining patterns of p53 and the need for correct interpretation of p53 IHC for the diagnosis of various EOT.

In 2020, Nayak S et al[53], conducted a study regarding immunohistochemical expression of p53 in serous carcinoma of ovary and its correlation. The study was carried over 18 histopathologically confirmed cases of serous carcinoma of ovary in VSSIMSR, Burla through a period of 1 year. Analysis of p53 expression was done immunohistochemically. The results of the study showed that out of total 18 cases of serous carcinoma, 14 cases were high grade serous carcinoma and 4 cases were low grade serous carcinoma. All the cases were in the age group of 40 to 60 years of age group. Out of 14 HGSOC cases, 11 cases (78.57%) were diagnosed in advanced stages (FIGO Stage III and IV)

while 3 out of 4 (75%) cases of LGSOC were diagnosed in comparatively earlier stages (FIGO stage I and II). Number of p53 positive cases in LGSOC was 2/4 (50%) and in HGSOC it was 14/14(100%), showing a statistically significant difference ($p<0.05$). Correlation analysis showed a strong positive correlation of p53 expression with grade of serous carcinoma (Spearman′ s rho correlation $\rho=0.701$, $p=0.001$). Higher level (3+, 4+, and 5+) and diffuse and patchy expression of p53 was expressed in HGSOC. The expression of p53 in LGSOC was focal reflected in low expression score (1+and 2+). They concluded that higher p53 expression mainly in high grade carcinoma suggests its prominent role in the pathogenesis of high grade serous carcinoma of ovary.

The present study was undertaken to observe the immunohistochemistry profile of ovarian neoplasms.

MATERIALS AND METHODS

The present 2 year study, 1 year retrospective (1st March 2020- 28th February 2021) and 1 year prospective (1st March 2021-28th February 2022) on Immunohistochemical spectrum of ovarian neoplasms was conducted in the Department of Pathology, Dayanand Medical College and Hospital, Ludhiana. All the histopathologically diagnosed ovarian neoplasms on which immunohistochemistry was done were included in the study. Slides were subjected to IHC examination under both low power (100x) and high power(400x).

Method of collection of data

Inclusion criteria

All ovarian neoplasms including primary and secondary neoplasms undergoing immunohistochemistry for definite categorization.

Exclusion criteria

All non ovarian neoplasms and any ovarian neoplasms on which immunohistochemistry was not been done.

Duration of study

This was two years study, conducted 1 year retrospective starting from 1st March 2020- 28th February 2021 and 1 year prospective starting from 1st March 2021-28th February 2022.

Study Design

This is prospective and retrospective study of 2 years duration.

Methodology

The tissue obtained in the histopathology laborartory was processed. Paraffin embedding and subsequent staining by Hematoxylin and Eosin was done. The slides were then subjected to histopathological examination. All 88 cases with diagnosis of ovarianneoplasms or metastasis to ovaries were subjected to immunohistochemical examination.

Hematoxylin and Eosin staining

The paraffin embedded tissue blocks cut at 2-3micron thickness by rotator microtome. Then the slides were kept on a hot plate in order to dewax the sections at temperature of 60 degree. Following this, the slides were deparaffinized in xylene, then hydrated through graded alcohol to water. Then it was stained with Harris hematoxylin for 15 minutes. The sections were washed well in running tap water until sections turned blue. The sections were then differentiated in 1% acid alcohol (1% HCL in 70% alcohol) for 5-10 seconds, washed well in tap water for 5 minutes or less. These were then stained with 1% eosin for 10 minutes followed by washing in running tap water for 1-5 minutes. Sections were dehydrated once again through graded alcohol, cleared xylene and mounted with DPX avoiding air bubbles.

Immunohistochemistry-standard strept avidin procedure

1. 2-3 um sections were cut and mounted on Poly-L-lysine coated slides. Slides were dried overnight at 37 degree C and dewaxed in xylene and hydrated.
2. Antigen retrieval procedure- The black box was filled 3/4th with citrate buffer and the slide carrier with slides was placed in it. The black box was placed in microwave for 9 minutes.
3. Boiling of the solution was observed and the microwave was reset for 6minutes and started.
4. The box was removed and cooled under tap water.
5. Blocking endogenous peroxidase - Sections were incubated at room temperature in 0.3% H_2O_2 in methanol for 30-45 minutes and rinsed in running tap water for 5-10 minutes and then dipped in distilled water for 1 minute.
6. The slides were placed in Tris buffer [only one change for 5 minutes].

7. Blocking reagent was applied for 5-10 min and excess of it was wiped off.
8. Primary antibodies were applied covering the whole section and incubated at room temperature for 1 hour.
9. Slides were then washed in Tris buffer for 5 minutes.
10. Ultra Vision One HRP polymer covering the whole tissue was applied and incubated at room temperature for 45 minutes.
11. Washing was done in TBS buffer [Tris buffer saline] for 5 minutes [4 changes].
12. One drop of substrate DAB [3, 3- Diaminobenzidine] solution was applied on each slide covering the whole material and incubated for 10- 15 minutes, then washed in deiodinized water.
13. Hematoxylin was applied for few seconds and washed under running water.
14. Them it was dried and dehydrated in alcohol and incubated for 2 minutes.
15. It was mounted in DPX [distyrenedibutyl phthalate xylene]

Immunohistochemistry- ventana benchmark gx procedure (automatic)

IHC staining of slides prepared from formalin fixed paraffin embedded tissue (FFPET) on the BenchMark Classic Automated system (from Ventana). Sections from FFPET biopsies were cut using the microtome at 3-4micron thickness and mounted onto SuperFrost Plus slides. For each slide, Ventana labels were then printed which included a unique barcode containing all protocol information. The slides were then loaded onto the BenchMark carousel and read by the Ventana Barcode Reader. The automated Benchmark system put the slides through a series of userdefined de-paraffinization and antigen retrieval steps before commencing with the antibody staining. The primary antibody was either applied automatically if in a pre-diluted dispenser or

otherwise manually titrated onto the slide. The pre-diluted dispensers of the ultraView Universal DAB Detection Kit then provided all reagents required for staining. The counterstain and post-counterstain comprised Hematoxylin [cat #760-2021] and bluing reagent [cat #760-2037]

Statistical Analysis

Data was described in terms of range, mean, median, frequencies (number of cases) and relative frequencies (percentages).

OBSERVATIONS AND RESULTS

The present 2 year study, 1 year retrospective (1st March 2020- 28th February 2021) and 1 year prospective (1st March 2021-28th February 2022) on Immunohistochemical spectrum of ovarian neoplasms was conducted in the Department of Pathology, Dayanand Medical College and Hospital, Ludhiana. All ovarian neoplasms including primary & secondary neoplasms undergoing immunohistochemistry for definite categorization were included in the study. The ovarian neoplasms which did not undergo immunohistochemistry test and all other neoplasms were excluded from the study. A total of 20998 specimens were received during this study period, out of which 198 were ovarian neoplasms and 88 cases were of ovarian neoplasms on which immunohistochemistry was done.

Distribution of types of specimens

In the present study, there were 88 cases of ovarian neoplasm. Maximum number of specimens were received as trucut biopsies (32/88; 36.6% cases). Second most common type of specimens were of total hysterectomy with bilateral salphingo-oopherectomy specimens (26/88; 29.5% cases) followed by unilateral oophorectomy (21/88; 23.8% cases) and bilateral oophorectomy specimens (5/88; 5.6% cases). In 4 cases outside blocks were received (4/88; 4.5% cases). In these 4 cases, a hysterectomy specimen with one sided ovary, 2 bilateral ovarian masses and one sided ovarian mass blocks were received on which immunohistochemistry was done.

Table 1- Distribution of types of specimens

Types of specimen	No. of specimens (n=88)	%age
Trucut biopsy	32	36.6
Total hysterectomy with bilateral salphingo-oopherectomy	26	29.5
Unilateral oophorectomy	21	23.8
Bilateral oophorectomy	5	5.6
Outside blocks	4	4.5

Gross examination

Distribution of cases according to tumour laterality

In the present study, most tumours involved unilateral ovary (75/88; 85.2% cases). Bilateral ovaries were involved in 13 cases (13/88; 14.7% cases).

Table 2- Distribution of cases according to tumour site

Tumour site	No. of cases (n=88)	%age
Unilateral	75	85.2
Bilateral	13	14.8

Age wise distribution of patients with ovarian neoplasms

In the present study, the age of presentation ranged from 15 to 74 years. It was observed that maximum ovarian neoplasms occurred in 6th decade of life (26/88; 29.6% cases), with the mean age of 49 years. The youngest patient was 15 years and oldest was 74 years old. There were no cases seen in 1st decade or after 8th decade of life.

Table 3- Age wise distribution of patients with ovarian neoplasms distribution of ovarian neoplasms according to WHO classification 2020

Age Range(years)	No. of patients(n=88)	%age
0-10	0	0
11-20	3	3.4
21-30	9	10.2
31-40	8	9.0
41-50	23	26.2
51-60	26	29.6
61-70	15	17.1
71-80	4	4.5

All the tumours were classified according to the WHO classification 2020 for ovarian neoplasms i.e; whether they belonged to epithelial, mesenchymal, sex cord stromal, germ cell tumours or metastasis from elsewhere in the body to the ovaries. Epithelial tumours formed the largest group with 56 cases (63.7%). Second most common type were sex cord stromal tumours comprising of 15 cases (17.0%) followed by metastatic tumours in 10 cases (11.3%), germ cell tumours 6 cases (6.8%). Least common were mesenchymal tumours comprising of 1 case (1.2%).

Table 4- Distribution of ovarian neoplasms according to WHO classification 2020

Types	No. of cases (n=88)	%age
Epithelial tumours	56	63.7
Sex cord stromal tumours	15	17.0
Metastasis	10	11.3
Germ cell tumours	6	6.8
Mesenchymal tumours	1	1.2

OVARIAN EPITHELIAL TUMOURS

Age wise distribution of ovarian epithelial tumours

In the present study, the age of presentation of ovarian epithelial tumours ranged from 22 to 74years. It was observed that maximumof 19 cases (34.0%) were seen in 6th decade of life. Least cases were seen in 3rd decade of life comprising of 2 cases (3.6%).

Table 5- Age wise distribution ovarian epithelial tumours

Age range (years)	No. of cases (n=56)	%age
0-10	0	0
11-20	0	0
21-30	2	3.6
31-40	6	10.7
41-50	15	26.8
51-60	19	34.0
61-70	11	19.6
71-80	3	5.3

IHC markers used for ovarian epithelial tumours

A combination of immunohistochemical markers were used to reach a final diagnosis. Depending on the morphology the markers used were WT1, ER, PR, PAX8, CK7, CK20, CK, CDX2, SATB2, Napsin A, GATA 3, p63, p53, p16, vimentin, inhibin, calretinin, CEA and EMA.

Distribution of ovarian epithelial tumours according to biological potential

In the present study out of 56 cases of ovarian epithelial tumours 52 (92.8%) were malignant, 1 was borderline (1.8%) and 3 (5.4%) were benign.

Table 6- Distribution of ovarian epithelial tumours according to biological potential

Category	No. of cases (n=56)	%age
Malignant	52	92.8
Benign	3	5.4
Borderline	1	1.8

Categories in ovarian epithelial tumours

Out of 56 ovarian epithelial neoplasm cases, maximum were serous carcinomas (34/56; 60.7%). Out of 34 serous carcinomas 30 were high grade and 4 were low grade. Second most common were endometrioid carcinomas (12/56; 21.5%). Out of 12 endometrioid carcinomas 1 was with seromucinous differentiation, one resembled sex cord tumours and one was of villoglandular type. These were followed by mucinous carcinomas (3/56; 5.4%), Brenner tumour (2/56; 3.5%). There were 1 case each of clear cell carcinoma, carcinosarcoma, seromucinous cystadenoma, serous borderline tumour and mesonephric like adenocarcinoma (1.8% cases each).

Table 7- Categories of ovarian epithelial tumours

Category	No. of cases (n =56)	% age
Serous carcinoma (34: 60.7%) High grade- Low grade-	 30 4	 53.6 7.1
Endometrioid carcinoma	12	21.4
Mucinous carcinoma	3	5.4
Brenner tumour	2	3.5
Clear cell carcinoma	1	1.8
Carcinosarcoma	1	1.8
Seromucinous cystadenoma	1	1.8
Serous borderline tumour	1	1.8
Mesonephric like adenocarcinoma	1	1.8

Serous carcinomas

Age wise distribution of serous carcinomas

In the present study there were 34 cases of serous carcinomas with maximum number of cases (11/34 cases) seen in 6th decade of life which was followed by 9 cases in 7th decade of life. Least number of cases were seen in 3rd and 8th decade of life (2/34 cases each).

Table 8- Age wise distribution of ovarian serous carcinomas

Age range (in years)	No. of cases (n=34)	%age
0-10	0	0
11-20	0	0
21-30	2	5.9
31-40	3	8.8
41-50	7	20.6
51-60	11	32.4
61-70	9	26.4
71-80	2	5.9

Distribution of serous carcinoma cases according to grade (In accordance with WHO classification of ovarian neoplasm 2020)

There were 34 cases of serous carcinomas out of 56 ovarian epithelial tumours (60.7%). On histopathological examination and immunohistochemistry they were classified as high grade (30/34 cases) and low grade (4/34 cases).

In the present study, 4 cases were reported as lowgrade serous carcinoma. On initial examination of these tumours 1 was rendered a provisional diagnosis of papillary neoplasm and in 3 cases it was reported as carcinoma likely low grade serous carcinomas. On doing immunohistochemical examination a final diagnosis of low grade serous carcinoma was made.

On histopathological examination, low grade serous carcinomas showed cellular tumours with cells arranged in nests and arborising papillae lined by cells having mild to moderate nuclear atypia (<3- fold variability in nuclear size), vesicular nuclei, conspicuous nucleoli and moderate amount of cytoplasm. Foci of invasion into stroma were noted. Mitosis <2-3/10hpf along with few psammoma bodies were seen.

On immunohistochemistry, in low grade serous carcinomas, WT1 and ER were diffuse positive in all 4 cases. p53 was focal weak positive in 3 cases and diffuse positive in 1 case but in this cases Ki 67 was 25%. PR and CK7 were applied in 1 case each and were focal and diffuse positive respectively.CK20 was applied in 1 case and was found to be negative. Ki 67 done in 2 cases was 25% and 30% respectively. Correlating histomorphology and immunohistochemistry findings a final diagnosis of low grade serous carcinoma was given in these 4 cases.

There were 30 cases of high grade serous carcinoma, 21 were provisionally diagnosed as carcinoma possibly high grade serous carcinoma, 6 as adenocarcinoma and 3 were diagnosed as papillary adenocarcinoma likely high grade. Immunohistochemistry was done in these cases and were diagnosed as high grade serous carcinoma

On histopathological examination high grade serous carcinomas, showed cellular tumours composed of solid masses of cells arranged in nests, sheets and focal papillae lined by large, markedly pleomorphic cells (nuclear size variability >3-fold), having hyperchromatic nuclei, prominent eosinophilic nucleoli and moderate amount of cytoplasm.

Invasion into stroma and brisk mitosis (>12/10 HPF) was noted. Foci of necrosis were evident in 19 cases (63.3% cases).

On immunohistochemistry in high grade carcinomas WT1 was diffuse positive in all 30 cases. In all 30 cases p53 was done and was found to be strong diffuse positive in 26 cases and null type in 4 cases. However, p16 was applied in these 4 cases and was diffuse strong positive. In total p16 was done in 12 cases and was diffuse positive. ER was applied in 25 cases and wasdiffuse positive in 20 cases, focal positive in 2 casesand negative in 3 cases. PR wasdone in 13 cases and was focal positive in 7 cases and negative in 6 cases. In 10 cases, CK7 was applied and was diffuse positive in all the cases. In 13 cases CK20 was done and was negative. PAX8 was applied and diffuse positive in 13 cases.

Table 9- Grade wise distribution of serous carcinomas

Grade	No. of cases (n=34)	% age
Low grade	4	11.7
High grade	30	88.3

Table 10- Immunohistochemistry in low grade serous carcinomas (n=4)

IHC markers	No. of cases in which IHC markers were applied	No. of cases positive	%age of positivity
WT1	4	4	100
ER	4	4	100
PR	1	1	100
p53	4	4	100
CK7	1	1	100
CK20	1	0	0
PAX8	2	2	100

Table 11- Immunohistochemistry in high grade serous carcinomas (n=34)

IHC markers	No. of cases in which IHC markers were applied	No. of cases positive	% age of positivity
WT1	30	30	100
P53 (Mutant)	30	30	100
ER	25	22	88
PR	13	7	53.8
P16	12	12	100
CK7	10	10	100
CK20	13	0	0
PAX8	15	15	100

In our study, WT1 was diffuse positive in all the cases of high and lowgrade serous carcinomas. p53 was found out to be focal weak positive (wild type) in low grade serous carcinomas and diffuse/null type positive (Mutant expression) with diffuse p16 expression in high

grade serous carcinomas. p53 mutant expression was found to be useful to diagnose a high grade serous carcinoma in the present study.

Mucinous carcinomas

Age wise distribution of mucinous carcinomas

In the present study there were 3 cases of mucinous carcinomas with one case each seen in 4^{th}, 6^{th} and 7^{th} decade of life.

Table 12- Age wise distribution of mucinous carcinomas

Age range (in years)	No. of cases(n=3)	%age
0-10	0	0
11-20	0	0
21-30	0	0
31-40	1	33.4
41-50	0	0
51-60	1	33.3
61-70	1	33.3
71-80	0	0

There were 3 cases that were provisionally diagnosed as mucinous carcinoma and after immunohistochemical testing these were rendered a final diagnosis of mucinous carcinomas and out of these one was diagnosed as mucinous carcinoma with intestinal differentiation.

On histomorphological examination, mucinous carcinomas exhibited cellular tumours in multiple cysts lined by tall columnar mucin secreting epithelium in papillae, focal glands >4 layers with minimal intervening

stroma creating labyrinth appearance. No capsular invasion was noted in any case.

On immunohistochemistry, CK20 and CK7 were done in 3 cases and were found to be positive. PAX8 was done and was negative in 2 cases and was not done in 1 case.WT1 was negative in all 3 cases. P53 was focal positive in all 3 cases. CDX2 was negative in 2 cases and positive in 1 case which was reported as mucinous carcinoma with intestinal differentiation. Napsin A was done in 1 case and was negative in which clear cell carcinoma was a differential diagnosis.

Table 13- Immunohistochemistry in mucinous carcinoma (n=3)

IHC markers	No. of cases in which IHC markers were applied	No. of cases positive	% age of positivity
CK20	3	3	100
CK7	3	3	100
CDX2	3	1	33.3
p53(focal)	3	3	100
PAX8	2	0	0
WT1	2	0	0
Napsin A	1	0	0

In our study we found combined positivity of CK7 and CK20 in mucinous carcinomas. CDX2 expression was seen with intestinal differentiation. WT1 and PAX8 were negative in the cases of mucinous carcinomas in which helped to differentiated low and high grade serous carcinomas. p53 was found to be focal positive in all 3 cases of mucinous carcinomas.

Endometrioid carcinomas

Age wise distribution of endometrioid carcinomas

In the present study, maximum number of ovarian endometrioid carcinoma cases were seen in 5th decade of life (6/12; 50% cases) followed by 6th decade of life (5/12; 41.6% cases) and 1 case was in 4th decade of life.

Table 14- Age wise distribution of endometrioid carcinomas

Age range (in years)	No. of cases (n=12)	% age
0-10	0	0
11-20	0	0
21-30	0	0
31-40	1	8.4
41-50	6	50
51-60	5	41.6
61-70	0	0

There were 9 cases which were provisionally diagnosed as adenocarcinoma likely endometrioid carcinoma and after immunohistochemistry were finally diagnosed as endometrioid carcinoma. One was diagnosed as highgrade adenocarcinoma possibly endometrioid carcinoma resembling sex cord stromal tumour and after immunohistochemistry was rendered a final diagnosis of endometrioid carcinoma resembling sex cord stromal tumour. One was diagnosed as adenocarcinoma with seromucinous differentiation which was finally diagnosed as endometrioid carcinoma with seromucinous differentiation after immunohistochemistry. One case was diagnosed as carcinoma possibly low grade serous carcinoma and after immunohistochemistry as this tumour was WT1 negative and diffuse

positive for ER and PR a final diagnosis of endometrioid carcinoma with villoglandular differentiation was rendered.

On histomorphological examination, endometrioid tumours showedback to back glandular arrangement with confluent or cribriform arrangement lined by stratified non mucinous epithelial cells with well defined luminal margins. Stromal invasion was noted. One tumour each, showed villoglandular type, sex cord stromal type, grade I and seromucinous differentiation, grade I. Foci of necrosis and atypical mitotic figures were noted. Out of these 12 cases, 8 were FIGO grade I and4 were FIGO grade II.

On immunohistochemistry, ER was found to be diffuse positive in all 12 cases. PR was diffuse positive in 10 cases and negative in 2 cases. In both these 2 cases ER was positive. Vimentin was found out to be positive in all cases. WT1 was negative in all the 12 cases. PAX8 was done in 9 cases and was positive in 8 cases, negative in 1 case. PAX8 and PR were negative in endometrioid carcinomas resembling sex cord stromal tumours. CK7 was done in 8 cases and was positive in 4 cases, negative in remaining 4 cases. p53 was positive in 6 cases (patchy positive in 4 cases and diffuse positive in 2 cases) and not done in 6 cases. p16 was focal positive in 3 cases and not done in 9 cases. CK done in 1 case was positive. CK20 was done in 1 case of seromucinous differentiation was focal weak positive. GATA3, CEA, SATB2 were done and negative in 1 case each. Inhibin and calretinin were done in endometrioid carcinoma resembling sex cord tumour and were negative. Napsin A was negative in 2 cases and one case was reported as endometrioid carcinoma with seromucinous differentiation. Ki67 was 8% in endometrioid carcinoma villoglandular type. So in our study all endometrioid carcinomas were found to be positive for vimentin, ER, PR and PAX 8, while WT1 was negative in all cases. p53 was wild type positive in all the cases.

Table 15- Immunohistochemistry in endometrioid carcinomas (n=12)

IHC markers	No. of cases in which IHC markers were applied	No. of cases positive	%age of positivity in cases
ER	12	12	100
PR	12	10	83.3
Vimentin	12	12	100
PAX8	9	8	88.8
CK7	8	4	50
CK20	1	1	100
P53	6	6	100
p16	3	3	100
CK	1	1	100
WT1	12	0	0
CEA	1	0	0
Inhibin	1	0	0
Calretinin	1	0	0
GATA3	1	0	0
Napsin A	2	0	0
CDX2	1	0	0
SATB2	1	0	0

In our study of ovarian endometrioid carcinomas, ER was positive in 100% cases as compared to PR which was positive in 83.3% cases. But the cases in which PR came out to be negative, ER was applied and was found out to be positive. CK7 was positive in only 50% cases as compared to 100% positivity seen in serous carcinomas (comparing the cases in which they were applied). WT1 was negative in all cases of endometrioid carcinomas (100% cases) as compared to 100% positivity seen in serous carcinomas.

Clear cell carcinoma

In the present study there was one case of clear cell carcinoma, seen in a 43 year old female. A provisional diagnosis of malignant neoplasm was given in this case and was finally diagnosed as clear cell carcinoma after immunohistochemistry.

On histomorphological examination, tumour cells were arranged in tubulocystic, papillary and solid pattern. Individual tumour cells showed moderate pleomorphic round to angulated vesicular nuclei with prominent nucleoli and moderate amount of clear cytoplasmwithhobnailing at places. Stromal hyalinisation and hyaline globules were noted. Areas of necrosis were seen. No capsular breech or lymphovascular invasion was noted.

On IHC, Napsin A came out to be strong diffuse positive along with p16 only in clear cell carcinoma as compared to other cases wherever these markers were applied.

Carcinosarcoma

In the present study, solitary case of carcinosarcoma was reported on immunohistochemistry in a 60 year old female in one case. A provisional diagnosis of malignant neoplasm was rendered in this case and after immunohistochemistry a final diagnosis of carcinosarcoma was given.

On histomorphological examination, a cellular tumour arranged in papillary configuration lined by large round cells having vesicular

nuclei, prominent nucleoli and moderate amount of cytoplasm were noted. Surrounding these, cells having spindled nuclei with pleomorphic vesicular chromatin and ill defined cytoplasm were seen. Focus of cartilage was also evident.

On immunohistochemistry, WT1, PAX8 and CK7 were positive in epithelial cells and vimentin was positive in spindle cells. OCT 4 was negative in both the components.

Mesonephric like adenocarcinoma

In this study there was 1 case of mesonephric like adenocarcinoma, seen in a 67 year old female. This case was rendered a diagnosis with immunohistochemistry.

On histomorphological examination, showed a cellular tumour with cells arranged in tubular and glandular configuration with solid configuration separated by ovarian stroma. Individual tumour cells had round nuclei with vesicular chromatin, inconspicuous nucleoli and moderate amount of cytoplasm with focal cytoplasmic clearing.

On immunohistochemistry, tumour cells were positive for CK, GATA3, and focal positive for CK7, Vimentin, focal weak positive for CK20, AR and weak positive for PAX8. Tumour cells were negative for WT1, ER, PR, P53, CDX2 and TTF1.

Seromucinous cystadenomas

In our study, one case of seromucinous cystadenoma in a female 38 years old was reported in which immunohistochemistry was done.

In this case, a provisional diagnosis of benign epithelial tumour with seromucinous differentiation was rendered which was proven after immunohistochemistry as seromucinous cystadenoma.

On histomorphological examination, cysts lined by a variable admixture of ciliated serous and tall mucin secreting cells with basally placed nuclei were seen. No hyperchromasia, nuclear stratification or invasion into stroma was noted.

Immunohistochemistry in seromucinous cystadenoma

Ciliated epithelial cells were positive for PAX8, WT1 and mucinous epithelial cells were positive for CK20. Tumour markers positive in both ciliated and mucinous epithelial cells were ER and CK7. CDX2 was negative in both types of cells.

Benign Brenner tumour

In the present study, 2 cases of benign Brenner tumour were reported on which immunohistochemistry was applied. The age of the patients was 58 and 72 years respectively.

Out of the 2 cases, one was given a final diagnosis of benign Brenner tumour as it was received with an immunohistochemistry request and the other one was diagnosed as neoplasm possibly Brenner tumour and was given a final diagnosis of benign Brenner tumour after applying IHC markers.

On histomorphological examination, a well circumscribed tumour arranged in oval irregular nests surrounded by abundant fibromatous stroma. Nests of transitional cells having bland oval nuclei with fine nuclear chromatin, conspicuous nucleoli, nuclear grooves and moderate amount of eosinophilic cytoplasm were noted. Few nests showed microcysts lined by low cuboidal to transitional epithelium were seen. However, no papillary growth, frequent mitosis, stromal invasion or capsular breech was identified.

On immunohistochemistry in Brenner tumour, p63 and CK7 were positive in both the cases. EMA, CEA, GATA3 and vimentin were appliedand were positive in 1 case. CK20 was applied on one case and was negative.

Table 16- Immunohistochemistry in Benign Brenner tumour (n=2)

IHC markers	No. of cases in which IHC markers were applied	No. of cases positive	%age of positivity in cases
P63	2	2	100
CK7	2	2	100
GATA3	2	1	50
EMA	2	1	50
CEA	2	1	50
Vimentin	2	1	50
CK20	1	0	0

In Brenner tumour, p63 and CK7 were positive in 100% cases. GATA3 and EMA were positive in 50% cases.

Serous borderline tumour

Out of 56 ovarian epithelial tumours, 1 case was diagnosed as serous borderline tumour, in a 49 year old female. In this case a provisional diagnosis of serous borderline tumour was given which was proved on immunohistochemistry.

On histomorphological examination, a cystic tumour was noted having hierarchial branching pattern with papillae formation. The papillary cores exhibited dense fibrous stroma and were lined by cells having vesicular nuclei, conspicuous nucleoli and moderate amount of cytoplasm. Nuclear stratification was noted. No lymphovascular/ perineural invasion/ capsular breech/ stromal invasion were noted.

On immunohistochemistry, WT1 and ER was diffuse positive, p53 was wild type positive and p16 was patchy positive.

SEX CORD STROMAL TUMOURS

There were 15 cases of sex cord stromal tumors in the present study.

Age wise distribution of sex cord stromal tumours

In the present study, the age of presentation of sex cord stromal tumours ranged from17 to 74 years. It was observed that maximum patients were seen in 3rd decade of life, with 4 cases (26.6%).

Table 17- Age wise distribution of sex cord stromal tumours

Age range (in years)	No. of cases (n=15)	%age of cases
0-10	0	0
11-20	1	6.7
21-30	4	26.6
31-40	1	6.7
41-50	3	20
51-60	2	13.3
61-70	3	20
71-80	1	6.7

Immunohistochemistry markers used in sex cord stromal tumours

A combination of immunohistochemical markers were used to reach a final diagnosis. The markers used were inhibin, calretinin, WT1, EMA, ER, vimentin, desmin, S100, PAX8 and others depending on the morphology of the tumour.

Reticulin stain was applied to differentiate between granulosa cell tumours and fibroma.

Categories in sex cord stromal tumours

Out of 15 cases of sex cord stromal tumours maximum cases belonged to adult granulosa cell tumour (8/15; 53.3 % cases). Second most common sex cord stromal tumour was fibroma (3/15; 20% cases) followed by Juvenile granulosa cell tumour (2/15; 13.3 % cases). Least common tumours were thecoma and Sertoli cell tumour (1/15; 6.7 % cases each).

Table 18- Categories in sex cord stromal tumours

Category	No. of cases (n=15)	%age of cases
Adult granulosa cell tumour	8	53.3
Fibroma	3	20
Juvenile granulosa cell tumour	2	13.3
Thecoma	1	6.7
Sertoli cell tumour	1	6.7

Adult granulosa cell tumour

Age wise distribution of Adult granulosa cell tumour

In the present study, maximum number of cases were seen in 5thdecade of life (3/8; 37.5% cases). Second most common age group was3rd decade (2/8; 25% cases) followed by one case each in 4th, 7th and 8th decade of life.

Table 19- Age wise distribution of Adult granulosa cell tumour

Age range (in years)	No. of cases (n=8)	%age of cases
0-10	0	0
11-20	0	0
21-30	2	25
31-40	1	12.5
41-50	3	37.5
51-60	0	0
61-70	1	12.5
71-80	1	12.5

There were 8 cases; out of which 5 were given a provisional diagnosis of sex cord stromal tumour possibly granulosa cell tumour and 2 cases were reported as suggestive of granulosa cell tumour. In one case outside blocks were received for immunohistochemistry. All 8 cases were rendered a final diagnosis of adult granulosa cell tumour after immunohistochemical stains.

On histomorphological examination, granulosa cell tumours were cellular and tumour cells were arranged in solid sheets, trabeculae, nests, macrofollicular and microfollicular patter. Individual tumour cells had round to oval nuclei, prominent nucleoli in few and moderate to abundant eosinophilic cytoplasm. Nuclear grooves were noted in few of the cells. Call - Exner bodies were seen. Cystic change was present. No high grade areas were noted in any of the tumours. However, no capsular invasion/nuclear atypia/ mitosis were noted. In 4 cases reticulin stain was done which highlighted tumour nests.

On immunohistochemistry, inhibin was found out to be focal positive in all 8 cases, calretinin was focal positive in 7 cases and diffuse positive in 1 case, WT1, in 3 cases was positive and in 5 cases it was negative, ER was positive in 1 case and not done in 7 cases. EMA applied in 4 cases was found to be negative. GATA3 was applied in 1 case and was negative. Chromogranin and synaptophysin were applied and negative in 1 case each.

Table 20- Immunohistochemistry in Adult granulosa cell tumour (n=8)

IHC markers	No. of cases in which IHC markers were applied	No. of cases positive	% age of positivity in cases
Inhibin	8	8	100
Calretinin	8	8	100
WT1	8	3	37.5
ER	1	1	100
EMA	4	0	0
GATA3	1	0	0
Chromogranin	1	0	0
Synaptophysin	1	0	0

It was observed in our study that inhibin and calretinin were consistently expressedin granulosa cell tumours with 100% positivity. However, WT1 was only positive in 37.5% cases, the positivity found was focal.

Fibroma

Age wise distribution of fibroma

In this study, 3 cases were seen in 3rd, 6thand 7th decade of life.

Table 21- Age wise distribution of fibroma

Age range (in years)	No. of cases (n=3)	%age
0-10	0	0
11-20	0	0
21-30	1	33.7
31-40	0	0
41-50	0	0
51-60	1	33.3
61-70	1	33.3

A provisional diagnosis of spindle cell neoplasm possibly sex cord stromal tumour – fibroma was given in all 3 cases which was proven with immunohistochemistry.

Histomorphological examination showed an encapsulated tumour composed of spindle to oval shaped cells with bland nuclei and scanty cytoplasm within a collagenised stroma. Focal areas of hemorrhage and necrosis were noted. No capsular breech/nuclear atypia/mitosis/ grooves were noted. Reticulin stain highlighted pericellular pattern.

On immunohistochemistry, SMA was positive in all 3 cases. WT1 was positive in 2 out of 3 cases. Vimentin and inhibin were each positive in one case out of 3 cases. Desmin and calretinin were negative in 3 cases. Desmin negativity ruled out the possibility of a leiomyoma in all

3 cases. S100 was applied in one case and was found to be negative. Ki 67 was done and was 10 % in one case.

Table 22- Immunohistochemistry in fibroma (n=3)

Markers applied	No. of cases in which IHC markers were applied	No. of positive cases	% age of positivity in cases
SMA	3	3	100
WT1	3	2	66.6
Vimentin	3	1	33.3
Inhibin	3	1	33.3
Calretinin	3	0	0
Desmin	3	0	0
S100	3	0	0

In the present study, fibromas showed 100% SMA positivity. Inhibin and calretinin showed 33.3% positivity and 0% positivity respectively. So SMA expression was consistently found in fibromas whereas inhibin and calretinin were found to be better markers for the diagnosis of granulosa cell tumours. Desmin negativity ruled out the differential diagnosis of a leimyoma.

Juvenile granulosa cell tumour

In the present study, 2 cases of juvenile granulosa cell tumour were reported in 17and 21 year old females. Out of the 2 cases one was reported as anaplastic variant of juvenile granulosa cell tumour.

In one of the case a provisional diagnosis of germ cell tumour possibly yolk sac tumour was rendered but after immunohistochemistry this tumour was negative for AFP, glypican 3, CD117, PLAP and positive for WT1, ER and calretinin. So a final diagnosis of juvenile granulosa

cell tumour was given. Second case was given a provisional diagnosis of sex cord stromal tumour which was proven after immunohistochemistry as anaplastic variant of juvenile granulosa cell tumour.

On histomorphological examination, a cellular tumour was seen arranged in predominantly reticular pattern, nesting, and follicles of varied morphology. The cells lining the follicles and in the solid areas had round nuclei without nuclear grooves and abundant eosinophilic but occasionally pale amphophilic cytoplasm. Pseudo-papillae lined by granulosa cells were seen in one case.

In anaplastic variant of juvenile granulosa cell tumour occasional survival pattern, extensive areas of necrosis, brisk mitosis and hyaline globules were also noted.

On immunohistochemistry, ER, WT1, calretinin were positive in both the cases. CK7 was applied on both the cases and was dot like positive in 1 case. Inhibin was applied on both the cases and was positive in 1 case. EMA was applied on one case and was negative. PLAP, PAX8, CD117, AFP, CD30, CDX2, chromogranin, synaptophysin, glypican were applied in both the cases and were negative. Ki67 was done and was 10% in juvenile granulosa cell tumour.

LCA, Heppar1 and S100 were applied in anaplastic variant of granulosa cell tumour and were negative.

Table 23- Immunohistochemistry in Juvenile granulosa cell tumour (n=2)

IHC markers	No. of cases in which IHC markers were applied	No. of positive cases	% age of positivity in cases
ER	2	2	100
WT1	2	2	100
Calretinin	2	2	100
Vimentin	1	1	100
EMA	1	0	0
CK7	2	1	50
Inhibin	2	1	50
PAX8	2	0	0
PLAP	2	0	0
AFP	2	0	0
CD117	2	0	0
CD30	2	0	0
CDX2	2	0	0
Glypican 3	2	0	0
Chromogranin	2	0	0
Synaptophysin	2	0	0

We noticed in our study that in juvenile granulosa cell tumour, calretinin was positive in 100% cases and inhibin was positive in 50% cases as compared to adult granulosa cell tumour in which both inhibin and calretinin were 100% positive. WT1 was positive in 100% cases of juvenile granulose cell tumours whereas in adult granulosa cell tumour WT1 was positive in 37.5% cases.

Thecoma

In this study, one case of thecoma was reported in a 69 year old female on which immunohistochemistry was applied. In this case a provisional diagnosis of sex cord stromal tumour was given which was proven as thecoma based on immunohistochemistry and morphology.

On histomorphological examination, a cellular tumour was seen having cells arranged in sheets. Individual tumour cells were round to oval with vesicular nuclei, conspicuous nucleoli, occasional nuclear grooves and moderate amount of cytoplasm. Few delicate blood vessels were seen. Reticulin stain highlighted pericellular pattern. On histomorphology it was differentiated from its close differential of fibroma as the tumor arrangement was in diffuse sheets whereas in fibromas they are present in intersecting fascicles. Individual tumors cells were round to oval wheres tumors cells in fibromas are spindled to ovoid present within variably collagenised stroma. In thecomas, occasional nuclear grooves can be seen whereas in fibromas no nuclear grooves are seen.

On immunohistochemistry, ER and inhibin were applied and were positive. Calretinin and PR were negative.

Sertoli cell tumour

One case of Sertoli cell tumour was reported in a 51 year old female.

Outside blocks were received of this case where they had kept the differential diagnosis of ? sex cord stromal tumour, ?? metastasis from an epithelial tumour. Immunohistochemistry was done and a final diagnosis of Sertoli cell tumour was rendered.

Histomorphological examination showed a tumour with cells arranged in nests separated by thin fibrovascular septae, trabecular arrangement and tubule formation. Individual tumour cells had round to oval nuclei, inconspicuous nucleoli and moderate amount of pale cytoplasm. Occasional mitotic figures were seen.

On immunohistochemistry, tumour cells were positive for CK, Vimentin, ER, PR and focal positive for inhibin.

Tumour cells were negative for PAX8, WT1, Melan A, EMA, TTF1, CK20, SATB2, SALL4, CEA and GATA3.

METASTATIC TUMOURS

Age wise distribution of metastatic tumours

In the present study, there were 10 tumours which metastasised to the ovaries. All the cases were recorded between 5th to 7thdecades of life. Maximum number of cases were seen in 5th decade of life (5/10; 50% cases).

Table 24- Age wise distribution of metastatic tumours

Age range (in years)	No. of cases (n=10)	%age
0-10	0	0
11-20	0	0
21-30	0	0
31-40	0	0
41-50	5	50
51-60	3	30
61-70	2	20

Immunohistochemistry markers used in metastatic deposits in ovary

A combination of markers was used based on morphology of the tumour or previous history of any carcinoma. Markers used were WT1, ER, PR, p53, p16, PAX8, Vimentin, HER 2/Neu, SMA, desmin, CD10, CD34, MUC1, CDX2, SATB2, CK20, CK7, P40 and GATA 3.

Distribution of metastatic tumours according to site of origin

In the present study, maximum number of cases were metastatic tumours from the uteri corpus (4/10; 40% cases) followed by breast (2/10; 20% cases). There was one tumour each from duodenum, endocervix, pancreas and appendix.

Table 25- Distribution of metastatic tumours according to site of origin

Site of origin	No. of cases(n=10)	%age
Uteri corpus	4	40
Breast	2	20
Duodenum	1	10
Pancreas	1	10
Endocervix	1	10
Appendix	1	10

On histomorphological examination, metastasised tumours showed morphology and immunohistochemistry similar to their primary site tumours.

There were 3 high grade serous carcinoma, endometrial in origin with metastatic deposits in ovary. Provisional diagnosis of high grade carcinoma was given in 2 cases and adenocarcinoma was rendered in 1 case. After immunohistochemistry a final diagnosis of high grade serous carcinomas, endometrial in origin with metastatic deposits in ovarywas given.

On histomorphological examination, tumour cells were arranged in nests and glandular configuration. Tumour cells showed marked nuclear pleomorphism, hyperchromatic nuclei and moderate amount of cytoplasm with many cells showing clear cytoplasm. On immunohistochemistry, WT1 was negative in all 3 cases thus ruling out ovarian serous carcinomas. Tumour cells were patchy positive for p53, diffuse positive for p16 and PR and PAX8 in all 3 cases. Vimentin was

applied in 1 case and was diffuse positive. ER was applied in all 3 cases and was positive in 1 case.

Table 26- Immunohistochemistry in endometrial high grade serous carcinomas, with metastatic deposits in ovary (n=3)

IHC markers	No. of cases in which IHC markers were applied	No. of cases in which positivity was seen	% age of positivity in cases
WT1	3	0	0
P53	3	3	100
P16	3	3	100
PAX8	3	3	100
PR	3	3	100
Vimentin	1	1	100
ER	3	1	33.3

So endometrial serous carcinomas were diagnosed by PAX 8, p16 and wild type p53 positivity and WT1 negativity, thus differentiating from serous ovarian carcinomas which are WT1 positive.

Table27- Immunohistochemistry in ovarian high grade serous carcinomas (n=30), endometrioid carcinomas (n=12) and high grade serous carcinomas, endometrial in origin with metastatic deposits in ovary (n=3)

Final diagnosis	WT 1 positivity	ER positivity
High grade ovarian serous carcinoma (n=30)	30/30 (100%)	22/25 (88%)
Endometrioid carcinoma (n=12)	0/12 (0%)	12/12 (100%)
High grade serous carcinomas, endometrial in origin with metastatic deposits in ovary (n=3)	0/3 (0%)	3/3(100%)

There was one case which was provisionally diagnosed as spindle cell neoplasm. After immunohistochemistry and based on morphology a final diagnosis of intravenous leiomyomatosis was rendered.

On histomorphological examination, metastatic deposits of intravenous leiomyomatosis- uterus to ovary showed numerous well circumscribed nodules composed of a tumour with cells arranged in fascicles, islands and around the vascular channels. Tumour cells had oval to elongated vesicular nuclei and moderate amount of cytoplasm. Occasional mitosis was noted. Tumour was present in lymphovascular spaces as well.

On immunohistochemistry, tumour cells were positive for SMA, Desmin, focal positive for CD10 and CD34 highlighted the vessel wall and vascular channels.

There were 2 metastatic tumours from the breast, one was lobular carcinoma. On histomorphology, one of the case showed infiltration by tumour cells arranged in single file pattern and cords. Tumour cells had monomorphic round nuclei and moderate cytoplasm. Other case showed extracellular pools of mucin amidst which were seen tiny clusters and singly scattered tumour cells having eccentric hyperchromatic nuclei and moderate amount of cytoplasm. Occasional tubule formation was noted.

On immunohistochemistry, in one case tumour cells were strong positive for GATA 3, ER and PR. Her2/Neu was negative. Ki67 was 8% in highest proliferating areas.

In other case, tumour cells were positive for ER, PR and GATA3. Her2/Neu was 1+. PAX 8 was negative in these tumour cells. E cadherin was lost in tumour cells.

Table 28- Immunohistochemistry in metastatic deposits of breast carcinoma to ovary (n=2)

IHC markers	No. of cases in which IHC markers were applied	No. of positive cases	% age of positivity in cases
ER	2	2	100
PR	2	2	100
Her2/Neu	2	1	50
PAX8	1	0	0

There was one case which was given a provisional diagnosis of adenocarcinoma, after immunohistochemistry which was given a final diagnosis of metastatic adenocarcinomatous deposits from duodenum to ovary.

On histomorphological examination, sections taken from the ovaries showed tumour cells arranged in glandular configuration and nests. Tumour cells had elongated nuclei with vesicular nuclei and moderate to abundant amount of cytoplasm.

On immunohistochemistry, tumour cells were positive for CDX2, CK7 and negative for PAX8, ER, WT1, CK20, SATB2.

Biopsy submitted from duodenal stricture biopsy along with ovarian biopsy showed similar histomorphological and immunohistochemistry profile.

There was one case which was given a provisional diagnosis of adenocarcinoma, after immunohistochemistry which was given a final diagnosis of metastatic adenocarcinomatous deposits of pancreas in ovary. Patient was a known case of ductal adenocarcinoma, pancreas.

On histomorphological examination, sections taken from the ovaries showed tumour cells arranged in glandular configuration, tubules and nests. Tumour cells had elongated nuclei with vesicular nuclei and moderate to abundant amount of cytoplasm.

On immunohistochemistry, tumour cells were positive for MUC 1, CK7, CEA and CDX2 and negative for CK20, PAX8, WT1 and ER.

There was one case which was given a provisional diagnosis of adenocarcinoma, after immunohistochemistry which was given a final diagnosis of endocervical adenocarcinomatous deposits (HPV related) to ovary. IHC was applied on cervical biopsy received of the same patient. It was reported as endocervical adenocarcinoma (HPV related). On histomorphological examination, there was a tumour arranged in glandular configuration and nests. Individual tumour cells exhibited nuclear hyperchromasia and stratification. Occasional mitosis was noted.

On immunohistochemistry, tumour cells were diffuse positive for p16, negative for ER, PR, WT1 and p40.

There was one case which was provisional diagnosed as mucinous carcinoma, after immunohistochemical testing it was finally diagnosed aslow grade appendiceal mucinous neoplasm with metastasis to ovaries. On histomorphological examination, there was a cellular tumour arranged in glandular configuration. Tumour cells showed hyperchromatic nuclei with moderate amount of cytoplasm. Interspersed goblet cells were noted. On immunohistochemistry, tumour cells were positive for CDX2 and CK20. Tumour cells were negative for CK7 and PAX8.

Sections submitted from appendix showed similar histomorphological and immunohistochemistry findings.

GERM CELL TUMOUR

Age wise distribution of germ cell tumour

In the present study, there were 6 cases of germ cell tumour. Maximum number of cases were seen in 3rd decade (3/6; 50% cases) followed by 2nd decade (2/6; 33.3% cases). One case was seen in 4th decade of life (1/6; 16.7% cases).

Table 29- Age wise distribution of germ cell tumour

Age range (in years)	No. of cases (n=6)	%age
0-10	0	0
11-20	2	33.3
21-30	3	50
31-40	1	16.7
41-50	0	0

Immunohistochemistry markers used for germ cell tumours

A combination of markers used was based on histomorphology and differential diagnosis. Markers used were PLAP, CD117, SALL4, OCT 4, CD30, AFP, glypican 3, CK, ER, CK7, CK20, PAX8 and WT1.

Categories of germ cell tumour

Out of 6 germ cell tumours 3 were dysgerminoma (50% cases) and 3 were yolk sac tumour (50% cases).

Table 30- Categories of germ cell tumour

Categories in germ cell tumour	No. of cases (n=6)	%age
Dysgerminoma	3	50
Yolk sac tumour	3	50

Dysgerminoma

There were 3 cases which were provisionally diagnosed as germ cell tumour possibly dysgerminoma in 2 cases and in one case 2 differentials were kept first of dysgerminoma and second of and embryonal carcinoma. In the latter case CD30 was negative so a final diagnosis of dysgerminoma was given in all 3 cases.

On histomorphological examination, there was a cellular tumour arranged in nests separated by fibrous septae. These fibrous septae were infiltrated by lymphocytes. Individual tumour cells were polygonal in shape with vesicular nuclei and moderate amount of cytoplasm.

On immunohistochemistry, PLAP, CD117 and OCT4 were positive in all 3 cases. SALL4 was positive in 2 cases. AFP was negative in 1 case. CD30 was done in all 3 cases and CK was done in 2 cases and were negative

Table 31- Immunohistochemistry in dysgerminoma (n=3)

IHC markers	No. of cases in which IHC markers were applied	No. of positive cases	% age of positivity in cases
CD117	3	3	100
PLAP	3	3	100
SALL4	2	2	100
OCT4	3	3	100
CD30	3	0	0
AFP	1	0	0
CK	2	0	0

CD117, PLAP and OCT4 showed 100% positivity in all cases. SALL4 was positive in both the cases it was applied. AFP, CD30 and CK were negative in all the cases in which they were applied and ruled out embryonal carcinoma and yolk sac tumour.

Yolk sac tumour

There were 3 cases in which a provisional diagnosis of germ cell tumour possibly yolk sac tumour was rendered which was finally diagnosed as yolk sac tumours after immunohistochemistry in the present study.

On histomorphological examination, there was a cellular tumour arranged in sheets exhibiting reticular pattern with cystic change. Individual tumour cells had moderate to marked nuclear pleomorphism,

vesicular nuclei and moderate amount of clear cytoplasm. Atypical mitotic figures and intrcytoplasmic hyaline globules were noted at places. No capsular breech was noted.

On immunohistochemistry, Glypican 3 was positive in all 3 cases. AFP was applied in 2 cases and was found to be positive in both the cases. SALL4 was applied and was positive in 1 case. PLAP and CD117 were applied in 1 case and were negative. ER, CK7, CK20, PAX8, WT1 were all applied and negative in one case. CD30 and OCT4 both were applied in one case and were negative.

Table 32- Immunohistochemistry in yolk sac tumour (n=3)

IHC markers	No. of cases in which IHC markers were applied	No. of positive cases	% age of positivity in cases
Glypican 3	3	3	100
AFP	2	2	100
SALL4	1	1	100
CD30	2	0	0
PLAP	1	0	0
CD117	1	0	0
OCT4	1	0	0
ER	1	0	0
CK7	1	0	0
CK20	1	0	0
PAX8	1	0	0
WT1	1	0	0

Glypican 3 was 100% positive in all 3 cases of yolk sac tumours. These cases were negative for CD117 and PLAP, in comparison to dysgerminoma which showed 100% positivity for these cases.

MESENCHYMAL TUMOURS

In the present study, there was one case of mesenchymal tumour which was given a provisional diagnosis of spindle cell neoplasm and when immunohistochemistry was applied a final diagnosisof leiomyoma was rendered.

On histomorphological examination, a cellular tumour arranged in intersecting fascicles of bland spindle cells with moderate amount of cytoplasm with cystic change along with focal areas of hyalinisation.

On immunohistochemistry, tumour cells were positive for SMA, Desmin and WT1. Tumour cells were negative for inhibin which ruled out the differential diagnosisof fibroma.

DISCUSSION

The optimal treatment and clinical outcome of ovarian neoplasms depend on establishing a correct diagnosis. Classically, histopathological examination has been the gold standard for tumor diagnosis. However, immunohistochemistry is extremely helpful in difficult cases where morphological features overlap. Immunohistochemistry is a convenient and effective tool to reach an accurate diagnosis for ovarian neoplasms and towards a specific histogenic origin of tumors. The lineage specific markers have proven to be specific and sensitive in many cases of histologically poorly differentiated malignancies.

The present 2 year study, 1 year retrospective (1st March 2020- 28th February 2021) and 1 year prospective (1st March 2021-28th February 2022) on Immunohistochemical spectrum of ovarian neoplasms was conducted in the Department of Pathology, Dayanand Medical College and Hospital, Ludhiana. All ovarian neoplasms including primary & secondary neoplasms undergoing immunohistochemistry for definite categorization were included in the study.

A total of 20998 specimens were received during this study period. Out of these 198 cases were of ovarian neoplasms. On 88 cases of ovarian neoplasms immunohistochemistry was done and were analysed with respect to light microscopic and immunohistochemical findings.

The age of patients in our study ranged from 15 years to 74 years, with a mean age of 49 years, alike study of Rambau PF et al[54] in which the mean age was 47.5 years. Another study, conducted by Kobel M at al[55] compared 3 cohorts with mean age of 61.2, 59.5, 56.8 years which is higher than the mean age in our study. Probable reason for this maybe the longer duration of their study (33 years). In our study, 51.2% patients were above 50 years which is analogous to study by Ho CM et al[56], where they found 57% patients above 50 years of age.

According to WHO classification 2020, maximum number of cases (63.7%) in our study belonged to epithelial ovarian tumours which is in concordance to study conducted by Ho CM et al[56] where they reported maximum number of epithelial tumours which comprised of 55% cases.Khan L et al[12] conducted a study in which 63.75% cases were of epithelial ovarian tumours andBatool A et al[57] in their study reported 63.08% as epithelial ovarian tumours.

In present study, according to biological potential of epithelial tumours, 92.8% were malignant followed by benign (5.4%) and borderline tumours (1.8%). However, Khan L et al[12], Ho CM et al[56], Batool A et al[57] and Modepalli N et al[58] found that maximum were benign ovarian tumours as shown in table 33. In our study maximum were malignant tumours as immunohistochemistry was done mostly in malignant cases and only those cases in which IHC was done were included in the study.

Table 33. Comparison of biological potential of epithelial ovarian neoplasms in various studies

Study	Benign	Borderline	Malignant
Present study	5.4%	1.8%	92.8%
Batool A et al	82%	2.8%	14.6%
Khan L et al	75%	0%	25%
Ho CM et al	68.9%	2.1%	28.9%
Modepalli N et al	83.%	4.9%	12.1%

Ovarian epithelial tumours

Numerically, ovarian epithelial tumours form the most important group of neoplasms out of which serous carcinomas form the largest group. In present study too, ovarian epithelial tumours were commonest ovarian tumours comprising of 56 cases, out of which 60.7% were serous carcinomas. Kriplani D et al[47] observed, 66.6% cases of serous carcinomas which is similar to our study. Comparable results were observed byKobel M et al[55] with 73.8% cases as serous carcinomas. Goel A et al[59] conducted a study in which serous carcinomas constituted 12.1% of epithelial ovariantumours.

Table 34- Comparison of distribution of ovarian epithelial tumours

Category	Present study(n=56/88)	Kriplani D et al (n=30)	Kobel M et al (n=1099)	Goel A et al (n=66)
Serous carcinomas	60.7%	66.6%	73.8%	12.1%
Endometrioid carcinoma	21.4%	-	9.2%	1.5%
Mucinous carcinoma	5.4%	13.4%	5.8%	4%
Brenner tumour	3.5%	3.4%	-	6%
Clear cell carcinoma	1.8%	3.4%	9%	-
Seromucinous cystadenoma	1.8%	-	-	-
Serous borderline tumour	1.8%	6.6%	-	7.5%
Mesonephric like adenocarcinoma	1.8%	-	-	-

In our study, 22- 74 years was found to be the age range for serous carcinomas which is similar to studies conducted by Naik PS et al[4] and Modepalli N et al[58] in which the age range was 14-76 years.

In our study, serous carcinomas were categorized into high grade and low grade serous carcinomas. WT1 is an IHC marker which invariably stains positive for serous carcinomas. In low grade serous carcinomas, p53 shows wild type immunoreactivity, in comparison to high grade serous carcinomas where p53 is mutant type. In present study, most sensitive markers for low grade and high grade serous carcinomas were found to be WT1 and p53. WT1 was found to be positive in all cases of low and high grade serous carcinomas. p53 showed wild type positivity in all cases of low grade serous carcinomas and mutant type positivity in high grade serous carcinomas.This is comparable to the studies conducted by Kaushil N et al[60], Sallum LF et al [61] and Kobel M et al[62] in table 35. Kaushil N et al[60] found, the expression of p53 with grade of tumour to be statistically in significant. Sallum LF et al[61] observed low-grade pattern (p53 staining in ≥1% of tumour cells and <70% of tumour cells and/or p53 complete absence + p16<90%of tumour cells) in 90.5% and 11.9% cases of low grade and high grade serous carcinomas respectively. High-grade pattern (p53 ≥70% of tumour cells or p53 complete absence + p16 ≥90% of tumour cells) was observed in 9.5% and 88.1% cases of low grade and high grade serous carcinomas respectively. ChatterjeeA et al[63] observed that 85.7% high grade serous carcinomas were positive for p53 as compared to 25% low grade serous carcinomas.

Table- 35 Comparison of sensitivity of IHC markers for serous carcinomas

Study	Low grade serous carcinomas			High grade serous carcinomas		
	WT1	**p53**	**p16**	**WT1**	**p53**	**p16**
Present study	100%	100%(wild)	-	100%	100%(mutant)	100%
Kaushik N et al	50%	0%	-	66.7%	100%	-
Sallum LF et al	71.4%	90.5%(wild) 9.5%(diffuse)	90.5% (patchy)	57.1%	98.8% (mutant)	58.5% (diffuse)
Kobel M et al	100%	100% (wild)	100% (patchy)	100%	100% (mutant)	100% (diffuse)
Chatterjee A et al	-	25%	-	-	85.7%	-

Mucinous neoplasms are less common as compared to serous neoplasms and these tumours are positive for CK20 (more so in intestinal type) and show negative immunostaining for WT1. In our study of 3 cases of mucinous carcinomas showed 100% positivity for CK7 and CK20. One case (33.3%) was positive for CDX2 which showed intestinal differentiation. Babaier A et al[64] observed that mucinous carcinomas were positive for CK7, CK20 and tumours with intestinal differentiation was positive for CDX2. Vang R et al[65] conducted a study, with findings similar to our study in which 100% cases were CK7 positive, 83% were CK20 positive and 40% were CDX2 positive. So in present study CK7 along with CK20 positivity was seen in mucinous neoplasms.

Endometrioid carcinoma comprises of 10%-15% of all primary ovarian carcinomas with coexistent endometriosis. These tumours are positive

for ER and show negative staining for WT1. In our study, endometrioid carcinomas constituted 21.4% (12/56) of ovarian epithelial tumours and 100% cases were positive for ER, Vimentin and 83.3% cases were positive for PR. All these cases were negative for WT1.So a combination of vimentin, ER and PR positivity along with WT1 negativity was found to be useful for diagnosis of endometrioid carcinoma of ovary in the present study. A similar study done by Khan L et al[12], had 2 cases of endometrioid carcinoma which showed 100% positivity for ER and PR. WT1 was negative in 100% cases. Atla B et al[66] conducted a study on 42 ovarian tumours out of which 3 were endometrioid carcinomas. ER and PR were positive in 66.7% cases (2/3).KaushikN et al[60] conducted a study on 78 epithelial ovarian tumours and 1 case was diagnosed as endometrioid carcinoma. This case was negative for WT1.

Clear cell carcinomas accounts for 10% of ovarian neoplasms. The tumour cells are large and some nuclei protrude into lumina giving a hobnail appearance. These tumours demonstrate Napsin A positivity and are negative for WT1. In our study, 1 case was diagnosed as clear cell carcinoma and it was diffuse positive for Napsin A. A study done by Skirnisdottir I et al[67] foundNapsin A positivity in 80% of ovarian clear cell carcinomas(12 out of 15 cases). Nili F et al[51] demonstrated 83% cases of ovarian clear cell carcinomas (35 out of 37) to be Napsin A positive. Findings similar to our study, were noted by Iwamoto M et al[68] with diffuse Napsin A positivity in 95.5% ovarian clear cell carcinoma cases. So positivity of Napsin A along with WT1 negativity and hobnail appearance on morphology were features of clear cell carcinoma ovary in the present study.

Carcinosarcomas are aggressive tumours with malignant epithelial and sarcomatous components. Sarcomatous element can be homologous or heterologous. Similar findings were observed in solitary case of carcinosarcoma, reported in our study. On histomorphology it was diagnosed with presence of epithelial component as papillary carcinoma which demonstrated WT1, CK7 and PAX8 immunoreactivity

and sarcomatous component was positive for vimentin. Similar to our study, Hollis RL et al[69] in 82 cases of ovarian carcinosarcomas showed 79.3% WT1 positivity in papillary carcinoma component and 20.7% were negative for WT1, which had endometrioid carcinoma component. Sarcomatous component was positive for markers such as vimentin, myogenin, desmin and S100. IHC in these cases was only helpful to highlight the epithelial and mesenchymal component and sub types of each component.

One case of mesonephric like adenocarcinoma was found in our study. This tumour was positive for CK, GATA 3, CK7, AR, PAX8, CK20 and negative for vimentin, WT1, ER, PR. p53, CDX2 and TTF1. A study conducted by Lee Y et al[70], on 5 cases of mesonephric like adenocarcinoma found PAX8 and GATA3 positivity in all 5 cases (100%). Four cases (80%) were positive for TTF1 and all (100%) were negative for WT1. ER was positive in 3 cases (60%) and PR in 1 case (20%). p53 was wild type positive in all cases (100%). McFarland M et al[71] studied 5 cases of mesonephric like adenocarcinoma. All 5 cases (100%) were positive for CK7, PAX8 and TTF1. GATA 3 was positive in 2 cases out of 4 (50%) in which it was applied. ER, PR and WT1 was negative in all cases (100%). In both the studies, GATA3 and PAX8 positivity with negative WT1were observed similar to our study. However, in our case TTF1 was negative. So based on histomorphology as well as AR, PAX8 positivity and negative WT1 helped us to render this diagnosis.

Seromucinous cystadenomas are benign ovarian neoplasms with admixture of 2 or more mullerian type epithelium, each accounting for 10% or more. One case of seromucinous cystadenoma was reported in our study, which was positive for WT1, PAX8 in ciliated cells and CK20 in mucinous cells. ER and CK7 were positive in both cell types. CDX2 was negative. Similar immunoprofile was observed by Nagamine M et al[72] in their study. Ciliated cells were positive for CK7, PAX8 and ER along with variable WT1 positivity whereas mucinous cells were

positive for CK20. Both the cells were negative for CDX2 thus ruling out the intestinal differentiation.

Brenners tumour comprises of 1 to 2% of ovarian neoplasms and average age of presentation being 50 years. These tumours are composed of epithelial nests which show immunoreactivity for keratins, CEA, EMA and nuclear GATA3. We had 2 cases of benign Brenners tumour. On immunohistochemistry, P63, CK7 showed 100% positivity, CEA and GATA3 showed 50% positivity. We found CK7 and p63 positivity a useful combination for diagnosis of Brenners tumour Roma AA et al[73] on study of 32 cases of Brenners tumour had 100% positivity for GATA3 whereas PAX8, PAX2 and SALL4 were negative in all cases. Both cases, in our study were diagnosed on the basis of 100% p63 positivity and GATA3 positivity in 1 case (50%). Comparable results to our study, were seen by Ordonez NG et al[40] in 8 cases of benign Brenners tumour with 100% cases positive for CK7 and 50% cases positive for CEA. All of their cases were negative for CK20.

Serous borderline tumours are categorised by cytological atypia and lack of invasion into stroma. Solitary case of serous borderline tumour was present in our study. Tumour cells were positive for WT1, ER, wild type positive for p53 and patchy positive for p16.Maniar KP et al[17] conducted a study, in which 19 cases of serous borderline tumour showed positivity for ER, PR and WT1, likewise our findings. Hauptmann Set al[74] discussed serous borderline tumours showed positivity for WT1, ER, PR, PAX8 and wild type p53, akin to our study.

Sex cord stromal tumours

Sex cord stromal tumours comprise approximately 5% of all ovarian neoplasms. These tumours include female type cells (granulosa and theca cells) and male type cells (Sertoli cells). In our study, there were 15 cases (17%) of sex cord stromal tumours with 26.6% cases in 3rd decade of life and age ranged from 17 – 74 years. Rambau PF et al[54] conducted a study, in which sex cord stromal tumours constituted 11.4% cases with mean age of 37 years. Similar to our study, Fayek IS

et al[75] observed age range from 13 – 84 years, in 77 patients of sex cord stromal tumours. A study by Haroon S et al[76] on 480 cases of sex cord stromal tumours,observed age rangeof 1 – 92 years, which is discordant from our study range. Probable reason may be the larger sample size in their study.

In our study out of 15 cases of sex cord stromal tumours, 8 (53.3%) were adult granulosa cell tumour and formed the largest group, followed by fibromas. Similar findings were observed by Fayek IS et al[75] in theirstudy of 77 patients of sex cord stromal tumours, in which 49.4% (38/77) were adult granulosa cell tumour. Haroon S et al[76] conducted a study on 480 cases of sex cord stromal tumours out of which maximum (211 cases, 43.9%) were granulosa cell tumours, alike our study findings. Rambau PF et al[54] in their study,noted that in both east African and alberta patientsadult granulosa cell tumour was 80% (24/30) and 70.6% (12/17) respectively and formed the majority of cases amongst sex cord stromal tumours. Deavers MT et al[30] conducted a study on 53 cases of sex cord stromal tumours in which 17 (32%) were adult granulosa cell tumour.

Granulosa cell tumours are composed of cells that resemble granulosa cells of a developing ovarian follicle. Based on the age of the patient, these are divided into adult type and juvenile type. Ninety five percent of granulosa cell tumours are of adult type. Inhibin has emerged as one of the most useful markers in diagnosing these tumours. However, calretinin is more sensitive but less specific than inhibin. In present study, there were 8 (53.3%) cases of adult granulosa cell tumour and 2 (13.3%) cases of juvenile granulosa cell tumour. All adult granulosa cell tumour cases (100%) were positive for inhibin, calretinin and 37.5% were positive for WT1. Findings similar to our study have been quoted in various studies. Deavers MT et al[30] conducted a study on 53 cases of sex cord stromal tumours, out of which 17(32%) were adult granulosa cell tumour. In these, calretinin was positive in 100% cases, inhibin was positive in 94% cases and WT1 was positive in 65% cases. Another study done by Guleria P et al[77], on 138 cases of sex cord

stromal tumours, out of which 57.2% were adult granulosa cell tumour. Out of these, IHC was done in 43 cases and 88.4% cases were positive for inhibin and the remaining 11.6% cases which were negative for inhibin, all showed positivity for calretinin. However, all of their cases (100%) were positive for calretinin, findings comparable to our study. Costa MJ et al[78] conducted a study on 137 cases of sex cord stromal tumours, out of which 58 (42.3%) were adult granulosa cell tumours which showed 100% positivity for inhibin.In a study by Cathro HP et al[33], 27 cases were of sex cord stromal tumours out of which 10 were granulosa cell tumours which showed 90%, 88%, 80% positivity for calretinin, WT1 and inhibin respectively, similar to our study results.

Juvenile granulosa cell tumour is diagnosed mostly in 2nd decade of life nearly in 80% of cases. Most patients present with isosexual precocity. Out of 2 cases of juvenile granulosa cell tumours in our study, 1 was reported as anaplastic variant. These were 100% positive for ER, WT1, calretinin, vimentin, 50% for CK7 and inhibin. Similar results were noted by Deavers MT et al[30] where 4 cases of juvenile granulosa cell tumours showed 100% positivity for inhibin, calretinin, CK and 50% positivity for WT1. Ye Y et al[79] also found similar results similar to our findings, with 7 cases of juvenile granulosa cell tumours being 100% positive for inhibin, vimentin, 85.7% positive for calretinin, ER and 42.8% being positive for WT1.

Certain sex cord stromal tumours arising in ovarian stroma are composed of either fibroblasts (fibroma) or plump spindle cells with lipid droplets (thecomas). These tumours account for 4 % of all ovarian tumours. In our study, 3 cases of fibroma were reported. On immunohistochemistry, all of the cases (100%) were positive for SMA, 66.6% were positive for WT1 and 33.3% were positive for inhibin. All the cases (100%) were desmin and calretinin negative. In a study byCathro HP et al[33], there were 7 (18.8%) cases of fibromas out of 27 cases of sex cord stromal tumours. On IHC, calretinin was positive in 29% cases, WT1 was positive in none of the cases (0%) and inhibin

was positive in 43% cases. Deavers MT et al[30] conducted a study on 53 cases of sex cord stromal tumours,in which 10 were fibromas which showed 100% positivity for calretinin, 80% for inhibin, 70% for WT1 and all cases were negative for EMA. Findings of these studies are discordant from our findings. However, our diagnosis was made on the basis of 100% SMA positivity, 66.6% WT1 positivity and negative desmin which helped us to rule out leiomyomas. A case reported by Chougule A et al[80], with findings similar to our study found that fibroma's spindle cells were positive for SMA and negative for desmin and h caldesmon.

We had 1 case of thecoma in our study. On immunohistochemistry, ER and inhibin were positive in this case. Calretinin and PR were negative. Deavers MT et al[30] in a study on 53 cases of sex cord stromal tumours, out of which 5 were diagnosed as thecomas showed 100% positivity for inhibin, calretinin, 20% positivity for WT1. A study done by Kommoss F et al[81] on 203 ovarian tumours, out of which 11 were thecomas and 10 (90.9%) were positive for inhibin, likewise our study findings.

Pure Sertoli cell tumours lack leydig cells and primitive stromal elements. Microscopically cells are arranged in tubular or follicle like pattern. There was single case of Sertoli cell tumour in our study and on IHC it was positive for CK, vimentin, ER, PR, focal positive for inhibin and negative for WT1 and EMA. A study was done by Zhao C et al[43] on 160 cases of ovarian tumours, in which 40 were Sertoli cell tumour. CK was positive in 65% of cases, ER in 8%, PR in 13%, inhibin in 98% and calretinin in 60% cases. EMA was negative in all cases. A study by Zhao C et al[82], on 26 cases of Sertoli cell tumours in which WT1 was applied, 25 cases (96%) showed positivity for WT1. Their findings are discordant to what we observed in our study and the reason maybe, more number of Sertoli cell tumour cases in their study.

Metastatic tumours

Ovary is one of the most common sites of metastasis. More than half of these are bilateral. The most common primary sites are stomach, large bowel, appendix, breast, uterus (corpus and cervix), pancreaticobiliary, gall bladder and lung. Immunohistochemistry play a major role in pin pointing the site of origin of tumour. Carcinomas with metastasis to ovaries are generally associated with poor prognosis. In our study, there were 10 cases (11.3%) of metastatic carcinomas to ovaries with most number of cases seen in 5th decade of life. Five (50%) out of 10 cases were from gynaecological sites, (4 (40%) from uteri corpus and 1 (10%) from endocervix). Findings comparable to our study, were noted byYada-Hashimoto N et al[83]in 64 cases of metastatic tumours to ovary and reported that 21.1% (64 out of 304) cases were of metastatic tumours to ovary with 40.6% (26) cases from gynaecological sites. Khunamornpong S et al[84], in their study found that 30% (170/473) cases were metastatic tumours to ovary with 31% (53) cases of gynaecological origin. Lee SJ et al[85] in their study, observed that metastatic ovarian malignancy accounted for 112 (13.6%) of the 821 ovarian malignancies and more than 70% were metastases from the gastrointestinal tract with colorectal cancer being the most common primary tumor. Their findings are discordant to our study, due to the larger sample size in their study.

In present study, there were 3 cases of endometrial high grade serous carcinoma with metastasis to ovary. All cases (100%) were negative for WT1 and 100% cases were positive for PR, p53 and p16. Goldstein NS et al[86] conducted a study on 18 cases of endometrial serous carcinomas, with 5 cases of metastasis. All these cases (100%) were negative for WT1 and positive for p53, with similar findings to our study.In a study done by Acs G et al[87], they found that WT1 was positive in 10 (62.5%) out of 16 serous endometrial carcinomas, findings that are discordant to our study. Similar study conducted with 31 cases of serous endometrial carcinomas by Egan JA et al[88] showed that 7.5% (2) cases were positive for WT1 and 83.9% (26) cases were

positive for p53. We found PR, p53 and p16 positivity along with WT1 negativity in metastatic tumours from uterus to ovaries.

In our study, there was 1 case of metastatic intravenous leiomyomatosis to ovaries which showed SMA, Desmin positivity, focal CD10 positivity and CD34 was highlighted around the blood vessels on immunohistochemistry. WuX et al[89] studied a case of intravenous leiomyomatosis with its metastasis to ovaries, heart and major blood vessels. These cells were positive for SMA, Desmin and CD34, likewise our study findings. S100 and LCA were negative.

In our study, there were 2 cases of metastatic breast carcinomas whichwere positive for GATA 3, ER, PR and negative for PAX8 which is similar to KubecekO et al[90] findings in which ER, PR and GATA3 were 100% positive in metastatic breast carcinomas. In our study, there was 1 case of metastatic adenocarcinomatous deposits from pancreas to ovary which showed positivity for MUC 1, CEA, CK7 and negative for PAX8, CK20, WT1 and ER. Comparable results were noted in their study, which showed diffuse strong positivity for CK7, CEA and MUC 5AC.

In present study, there was 1 case of endocervical adenocarcinomatous deposits to ovary (HPV related) which showed diffuse strong positivity for p16. ER, PR, WT1 and p40 was negative in our case. In concordance with our findings, KubecekO et al[90] in their study noted that these tumours were positive for p16 and negative for ER and PR. There was 1 case of low grade appendiceal mucinous neoplasm with metastasis to bilateral ovaries in present study which was positive for CDX2, CK20 and negative for CK7 and PAX8. Our findings are similar to Kubecek O et al[90] study which showed positivity for CK20, CEA and CK7 negativity.

Vang R et al[25] did a study with 179 cases of ovarian tumours and found that 25 cases of colorectal carcinoma were 88% positive for CDX2 and 92% positive for CK20. In their study, there were 4 cases of metastatic appendiceal neoplasms and 100% cases showed CDX2

and CK20 immunoreactivity. Their study findings are similar to our study.

A study done by Kriplani D et al[47] on 37 cases of ovarian tumours found 7 cases of metastatic ovarian tumours, 4 from colorectum and 3 from endometrium. In their study, they found that 75% (3 cases) of metastatic colorectal carcinomas were negative for CK7, 75% cases were positive for CEA and 100% were positive for CK20. None of the cases (0%) of metastatic endometrial serous carcinomas were positive for WT1.

Germ cell tumours

Germ cell tumours constitute approximately 20% of all ovarian tumours. Most of these are seen in children and young adults. Dysgerminomas forms less than 1% of all ovarian neoplasms. Dysgerminomas shows consistent immunoreactivity for CD117 and PLAP. Yolk sac tumours show positivity for AFP and Glypican 3, in most of the cases. In our study, there were 6 cases of germ cell tumours, comprising of 3 cases each of dysgerminoma and yolk sac tumour. CD117 and PLAP were found to be useful markers for diagnosis of dysgerminomas in our study. All 3 cases of dysgerminoma were 100% positive for CD117, PLAP, OCT4 and SALL4 was applied in 2 cases and it showed 100% positivity and AFP was applied in one case and it was negative. Similar results were seen in a study by Gica N et al[91], where all cases of dysgerminoma were positive for CD117, OCAT3/4, negative for AFP and Glypican 3. Another study, with findings comparable to our study, was conducted on 15 cases of dysgerminoma, by Lifschitz-Mercer B et al[92] and found that 93.3% cases (14 cases) were positive for PLAP. Similar findings were encountered by Teng L H et al[93] in which a study on 7 cases of dysgerminoma found that 85.7% cases(6 cases) were positive for OCT4, 71.4% cases (5 cases) were positive for CD117 and all cases were negative for CD30, which is analogous to our study.

In our study Glypican 3 and AFP were found to be useful markers for diagnosis of yolk sac tumours. All cases of yolk sac tumours showed 100% positivity for Glypican 3. AFP was applied in 2 cases and showed 100% positivity. These tumours were negative for CD117, OCT4 and SALL4. Gica N et al[91] found that yolk sac tumours were positive for AFP, Glypican 3, negative for CD117 and negative for OCT3/4 in all of the cases, which is similar to our study. A study by Teng LH et al[93] on 6 cases of yolk sac tumours, only 1 case each showed weak positivity for PLAP and CD117. Comparable results to our study were noted by Chaudhary RK et al[94] where all 7 cases (100%) of yolk sac tumours in their study were positive for AFP. Zynger D L et al[95] in their study on yolk sac tumours applied Glypican 3 and AFP in 39 and 24 cases respectively. They found that 100% cases expressed Glypican 3 and 58% cases expressed AFP with focal staining at places.

Mesenchymal tumours

Leiomyomas accounts for 0.5-1% of all benign ovarian tumours and may be associated with synchronous leiomyomas of uterus. In our study, there was solitary case of leiomyoma based on immunohistochemistry and by ruling out the differential diagnosis of fibroma. This tumour was positive for SMA, Desmin and WT1.Inhibin was negative in this case. Socombination of SMA and Desmin was found to be useful for diagnosis of leiomyoma. Fibroma was ruled out by Desmin positivity. Lerwill MF et al[96] in their study reported 22 cases as leiomyomas. They reported these cases based on the presence of cigar shaped nuclei cells and these cells were positive for Desmin and SMA. Their findings were similar to our findings.

The limitation of our is less number of ovarian tumours. Although the number of ovarian tumours received to our histopathology department were more but immunohistochemistry was done only in 88 cases. The reason being, immunohistochemistry was mainly done in the malignant tumours of the ovary.

Future prospectives of our study is that a set panel of immunohistochemical markers depending on morphological features must be followed for definite categorisation of ovarian tumours.

SUMMARY AND CONCLUSIONS

This study was conducted in Dayanand Medical College and Hospital, Ludhiana, over a period of two years (March 2020- February 2022). A total of 88 histologically diagnosed ovarian tumours were examined with respect to their immunohistochemical findings.

The following features were highlighted in this study:

- During the study period a total of 20998 specimens were received for histopathological examination in our department. Out of these, 88 cases of ovarian neoplasms were analysed with respect to light microscopy and immunohistochemical findings.
- The age of patients in our study ranged from 15 years to 74 years, with a mean age of 49 years. Maximum ovarian neoplasms occurred in 6^{th} decade of life.
- Epithelial tumours formed the largest group with 56 cases (63.7%). Second most common type were sex cord stromal tumours comprising of 15 cases (17.0%) followed by metastatic tumours in 10 cases (11.3%), germ cell tumours 6 cases (6.8%). Least common were mesenchymal tumours comprising of 1 case (1.2%).
- According to the biological potential ovarian epithelial tumours comprised of 92.8% malignant tumours, 5.4% benign tumours and 1.8% borderline tumours.
- Ovarian epithelial tumours comprised of 60.7% serous carcinomas which formed the largest group followed by 21.5% endometrioid carcinomas, 5.4% mucinous carcinomas and clear cell carcinoma, carcinosarcoma, seromucinous cystadenoma, serous borderline tumour and mesonephric like adenocarcinoma comprising of 1.8% cases each.
- Amongst low grade serous carcinomas, WT1 and ER showed 100% positivity in all cases. Wild type staining pattern of p53 was observed in all cases.

- WT1 positivity and mutant type p53 was found consistently positive in all 34 cases of high grade serous carcinomas. Twenty six cases showed diffuse staining pattern of p53 and 4 cases showed null type staining pattern. These 4 cases showed diffuse strong staining of p16.
- CK7 and CK20 were found consistently positive in all 3 cases of mucinous carcinomas. CDX2 positivity was seen in one case of mucinous carcinoma with intestinal differentiation. PAX8 was found to be negative.
- Endometrioid carcinomas showed 100% positivity for ER and vimentin. PR was found positive in 83.3% cases. CK 20 was positive in endometrioid carcinoma with seromucinous differentiation.
- Clear cell carcinoma showed diffuse strong positivity for Napsin A and p16.
- Carcinosarcoma was a biphasic tumour and showed WT1, PAX8 and CK7 positivity in epithelial cells. Vimentin positivity was seen in spindle cells.
- Seromucinous cystadenoma showed positivity for PAX8, WT1 in ciliated cells and CK20 positivity in mucinous cells. ER and CK7 were positive in both type of cells.
- Benign Brenners tumour showed consistent positivity for p63 and CK7.
- Serous borderline tumour showed diffuse positivity for WT1, ER and wild type positivity for p53. p16 was found to be patchy positive.
- Sex cord stromal tumours comprised of maximum number of adult granulosa cell tumours (53.3%), followed by fibroma (20%) and juvenile granulosa cell tumours (13.3%). Thecoma and Sertoli cell tumour comprised of 6.7% cases each.
- Adult granulosa cell tumours were consistently positive for inhibin and calretinin (100%). However, WT1 was positive in 37.5% cases only.

- All cases of fibroma were 100% sensitive for SMA. 66.6% cases were positive for WT1. Vimentin and inhibin were positive in only 33.3% cases.
- Juvenile granulosa cell tumours were found to be consistently positive for ER, WT1 and calretinin. CK7 and inhibin were positive in only 50% cases.
- Thecoma showed positivity for ER and inhibin. Calretinin and PR were negative in this case.
- Sertoli cell tumour was positive for CK, vimentin, ER, PR and focal positive for inhibin.
- Metastatic tumours to ovary comprised of 10 cases. maximum number of cases were from uteri corpus (40%), followed by breast (20%). Metastatic tumours from duodenum, pancreas, endocervix and appendix comprised of 10% caes each.
- Metastatic endometrial high grade serous carcinoma to ovaries showed consistent WT1 negativity in all cases.
- Metastasis of intravenous leiomyomatosis to ovary showed immunopositivity for SMA, Desmin and focal CD10. CD34 highlighted the vessel walls and vascular channels.
- Metastatic breast carcinomas to ovary showed ER, PR and GATA 3 positivity. One case was diagnosed as lobular breast carcinoma with metastasis to ovary, which showed E Cadherin negativity.
- Metastatic adenocarcinomatous deposits from duodenum to ovary showed CDX2 and CK7 positivity. However, it was negative for PAX8, ER, WT1, CK20 and SATB2.
- Metastatic adenocarcinomatous deposits of pancreas in ovary showed immunopositivity for MUC 1, CK7, CEA, CDX2 and it was negative for CK20, PAX8, WT1 and ER.
- Endocervical adenocarcinomatous deposits (HPV related) showed diffuse immunopositivity for p16. However, this was negative for ER, PR, WTI and P40.

- Low grade appendiceal mucinous neoplasm with metastasis to ovaries showed immunopositivity for CDX2 and CK20. This were negative for for CK7 and PAX8.
- Germ cell tumours consisted of 50% cases of dysgerminoma and 50% cases of yolk sac tumour
- Dysgerminomas were consistently positive for CD117, PLAP, OCT4 and SALL4.
- Yolk sac tumours showed Glypican 3 positivity in all the cases. AFP was positive in both the cases in which it was applied.
- Mesenchymal tumours comprised of 1 case of leiomyoma and it showed immunopositivity for SMA, Desmin and WT1. It was negative for inhibin.

BIBLIOGRAPHY

1. Devi VS. Inderbir Singh's Human Embryology. 11th ed. New Delhi, India: Jaypee Brothers Medical; 2018;25-43.
2. Goldblum JR, Lamps LW, McKenney J, Myers JL. Rosai and Ackerman's Surgical Pathology E-Book 11th ed. Elsevier Health Sciences; 2017;1367-1415.
3. Ellenson LH, Pirog EC. The female genital tract chapter 22. Robbins and Cotran Pathologic Basis of Disease. 10th Eds. Editor Kumar Abbas Fausto Aster. Philadelphia: Saunders Elsevier. 2010;.985-1035
4. Naik PS, Deshmukh S, Khandeparkar SG, Joshi A, Babanagare S, Potdar J, et al. Epithelial ovarian tumors: Clinicopathological correlation and immunohistochemical study. Journal of Mid-life Health. 2015;6:178.
5. Basu P, De P, Mandal S, Ray K, Biswas J. Study of 'patterns of care'of ovarian cancer patients in a specialized cancer institute in Kolkata, eastern India. Indian journal of cancer. 2009;46:28-33.
6. Muñoz N, Franceschi S, Bosetti C, Moreno V, Herrero R, Smith JS, et al. Role of parity and human papillomavirus in cervical cancer: the IARC multicentric case-control study. The Lancet. 2002;359:1093-101.
7. Singh N, Gilks CB, Wilkinson N, McCluggage WG. The secondary Müllerian system, field effect, BRCA, and tubal fimbria: our evolving understanding of the origin of tubo-ovarian high-grade serous carcinoma and why assignment of primary site matters. Pathology. 2015;47:423-31.
8. Shah SP, Köbel M, Senz J, Morin RD, Clarke BA, Wiegand KC, et al. Mutation of FOXL2 in granulosa-cell tumors of the ovary. New England Journal of Medicine. 2009;360:2719-29.
9. Clarke BA, Witkowski L, Ton Nu TN, Shaw PA, Gilks CB, Huntsman D, et al. Loss of SMARCA4 (BRG1) protein expression as determined by immunohistochemistry in small-cell carcinoma of the

ovary, hypercalcaemic type distinguishes these tumours from their mimics. Histopathology. 2016;69:727-38.
10. Taylor J, McCluggage WG. Ovarian seromucinous carcinoma. The American journal of surgical pathology. 2015;39:983-92.
11. Sylvia MT, Kumar S, Dasari P. The expression of immunohistochemical markers estrogen receptor, progesterone receptor, Her-2-neu, p53 and Ki-67 in epithelial ovarian tumors and its correlation with clinicopathologic variables. Indian journal of pathology and microbiology. 2012;55:33.
12. Khan L, Arora A, Agarwal A, Pantola C, Kala S, Rathi RK, et al. Role of immunohistochemistry in ovarian tumors. Journal of Evolution of Medical and Dental Sciences. 2014;3:2814-20.
13. Cartun RW, Taylor CR, Dabbs DJ. Techniques of immunohistochemistry: principles, pitfalls, and standardization. Diagnostic Immunohistochemistry E-Book: Theranostic and Genomic Applications. 2021:1-50.
14. Seidman JD, Soslow RA, Vang R, Berman JJ, Stoler MH, Sherman ME, et al. Borderline ovarian tumors: diverse contemporary viewpoints on terminology and diagnostic criteria with illustrative images. Human pathology. 2004;35:918-33.
15. Seidman JD, Kurman RJ. Ovarian serous borderline tumors: a critical review of the literature with emphasis on prognostic indicators. Human pathology. 2000;31:539-57.
16. Bell DA, Scully RE. Ovarian serous borderline tumors with stromal microinvasion: a report of 21 cases. Human pathology. 1990;21:397-403.
17. Maniar KP, Wang Y, Visvanathan K, Shih IM, Kurman RJ. Evaluation of microinvasion and lymph node involvement in ovarian serous borderline/atypical proliferative serous tumors. A Morphologic and Immunohistochemical Analysis of 37 Cases. The American journal of surgical pathology. 2014;38:743.
18. Bárcena C, Oliva E. WT1 expression in the female genital tract. Advances in Anatomic Pathology. 2011;18:454-65.

19. Seidman JD, Kurman RJ. Subclassification of serous borderline tumors of the ovary into benign malignant types: a clinicopathologic study of 65 advanced stage cases. The American journal of surgical pathology. 1996;20:1331-45.
20. Yemelyanova A, Mao TL, Nakayama N, Shih IM, Kurman RJ. Low-grade serous carcinoma of the ovary displaying a macropapillary pattern of invasion. The American journal of surgical pathology. 2008;32:1800.
21. Malpica A, Deavers MT, Lu K, Bodurka DC, Atkinson EN, Gershenson DM, et al. Grading ovarian serous carcinoma using a two-tier system. The American journal of surgical pathology. 2004;28:496-504.
22. Zivanovic O, Sima CS, Iasonos A, Bell-McGuinn KM, SabbatiniPJ, Leitao MM et al. Exploratory analysis of serum CA-125 response to surgery and the risk of relapse in patients with FIGO stage IIIC ovarian cancer. Gynecologic oncology. 2009;115:209-14.
23. Yemelyanova AV, Vang R, Judson K, Ronnett BM. Distinction of primary and metastatic mucinous tumors involving the ovary: analysis of size and laterality data by primary site with reevaluation of an algorithm for tumor classification. The American journal of surgical pathology. 2008;32:128-38.
24. Rodríguez IM, Prat J. Mucinous tumors of the ovary: a clinicopathologic analysis of 75 borderline tumors (of intestinal type) and carcinomas. The American journal of surgical pathology. 2002;26:139-52.
25. Vang R, Gown AM, Barry TS, Wheeler DT, Yemelyanova A, Seidman JD, et al. Cytokeratins 7 and 20 in primary and secondary mucinous tumors of the ovary: analysis of coordinate immunohistochemical expression profiles and staining distribution in 179 cases. The American journal of surgical pathology. 2006;30:1130-9.
26. Köbel M, Kalloger SE, Huntsman DG, Santos JL, Swenerton KD, Seidman JD et al. Differences in tumor type in low-stage versus

high-stage ovarian carcinomas. International Journal of Gynecological Pathology. 2010;29:203-11.

27. Mostoufizadeh M, scully RE. Malignant tumors arising in endometriosis. Clinical obstetrics and gynecology. 1980;23:951-63.
28. Kato N, Takeda J, Fukase M, Motoyama T. Alternate mucoid and hyalinized stroma in clear cell carcinoma of the ovary: manifestation of serial stromal remodeling. Modern Pathology. 2010;23:881-8.
29. Esheba GE, Longacre TA, Atkins KA, Higgins JP. Expression of the urothelial differentiation markers GATA3 and placental S100 (S100P) in female genital tract transitional cell proliferations. The American journal of surgical pathology. 2009;33:347-53.
30. Deavers MT, Malpica A, Liu J, Broaddus R, Silva EG. Ovarian sex cord-stromal tumors: an immunohistochemical study including a comparison of calretinin and inhibin. Modern Pathology. 2003;16:584-90.
31. Hayes MC, Scully RE. Ovarian steroid cell tumors (not otherwise specified): a clinicopathological analysis of 63 cases. Obstetrical &Gynecological Survey. 1988;43:314-7.
32. Jones MW, Harri R, Dabbs DJ, Carter GJ. Immunohistochemical profile of steroid cell tumor of the ovary: a study of 14 cases and a review of the literature. International Journal of Gynecological Pathology. 2010;29:315-20.
33. Cathro HP, Stoler MH. The utility of calretinin, inhibin, and WT1 immunohistochemical staining in the differential diagnosis of ovarian tumors. Human pathology. 2005;36:195-201.
34. Mooney EE, Nogales FF, Bergeron C, Tavassoli FA. Retiform Sertoli–Leydig cell tumours: clinical, morphological and immunohistochemical findings. Histopathology. 2002;41:110-7.
35. Dietl J, Horny HP, Ruck P, Kaiserling E. Dysgerminoma of the ovary an immunohistochemical study of tumor-infiltrating lymphoreticular cells and tumor cells. Cancer. 1993;71:2562-8.
36. Liu X, Zhang X, Pang Y, Ma Y, Zhang X, Liu P. Clinicopathological factors and prognosis analysis of 39 cases of non-gestational

ovarian choriocarcinoma. Archives of gynecology and obstetrics. 2020;301:901-12.

37. Rabban JT, Zaloudek CJ. A practical approach to immunohistochemical diagnosis of ovarian germ cell tumours and sex cord–stromal tumours. Histopathology. 2013 ;62:71-88.
38. Oliva E, Garcia-Miralles N, Vu Q, Young RH. CD10 expression in pure stromal and sex cord-stromal tumors of the ovary: an immunohistochemical analysis of 101 cases. International Journal of Gynecological Pathology. 2007;26:359-67.
39. Kunkel J, Peng Y, Tao Y, Krigman H, Cao D. Presence of a sarcomatous component outside the ovary is an adverse prognostic factor for primary ovarian malignant mixed mesodermal/mullerian tumors: a clinicopathologic study of 47 cases. The American Journal of Surgical Pathology. 2012;36:831-7.
40. Ordónez NG, MacKay B. Brenner tumor of the ovary: a comparative immunohistochemical and ultrastructural study with transitional cell carcinoma of the bladder. Ultrastructural Pathology. 2000;24:157-67.
41. Logani S, Oliva E, Arnell PM, Amin MB, Young RH. Use of novel immunohistochemical markers expressed in colonic adenocarcinoma to distinguish primary ovarian tumors from metastatic colorectal carcinoma. Modern pathology. 2005;18:19-25.
42. Netinatsunthorn W, Hanprasertpong J, Dechsukhum C, Leetanaporn R, Geater A. WT1 gene expression as a prognostic marker in advanced serous epithelial ovarian carcinoma: an immunohistochemical study. BMC cancer. 2006;6:1-9.
43. Zhao C, Bratthauer GL, Barner R, Vang R. Comparative analysis of alternative and traditional immunohistochemical markers for the distinction of ovarian sertoli cell tumor from endometrioid tumors and carcinoid tumor: A study of 160 cases. Am J SurgPathol. 2007;31:255-66.
44. Cao D, Guo S, Allan RW, Molberg KH, Peng Y. SALL4 is a novel sensitive and specific marker of ovarian primitive germ cell tumors and is particularly useful in distinguishing yolk sac tumor from clear

cell carcinoma. The American journal of surgical pathology. 2009;33:894-904.

45. Shin JH, Bae JH, Lee A, Jung CK, Yim HW, Park JS, et al. Immunohistochemical staining used to distinguish metastatic colorectal carcinoma involving ovary from primary ovarian mucinous adenocarcinoma. Japanese journal of clinical oncology. 2010;40:208-13.
46. Giurgea LN, Ungureanu C, Mihailovici MS. The immunohistochemical expression of p53 and Ki67 in ovarian epithelial borderline tumors. Correlation with clinicopathological factors. Rom J MorpholEmbryol. 2012;53:967-73.
47. Kriplani D, Patel MM. Immunohistochemistry: A diagnostic aid in differentiating primary epithelial ovarian tumors and tumors metastatic to the ovary. South Asian journal of cancer. 2013;2:254-8.
48. Cole AJ, Dwight T, Gill AJ, Dickson KA, Zhu Y, Clarkson A, et al. Assessing mutant p53 in primary high-grade serous ovarian cancer using immunohistochemistry and massively parallel sequencing. Scientific reports. 2016;6:26191.
49. Rekhi B, Deodhar KK, Menon S, Maheshwari A, Bajpai J, Ghosh J, et al. Napsin A and WT 1 are useful immunohistochemical markers for differentiating clear cell carcinoma ovary from high-grade serous carcinoma. Apmis. 2018;126:45-55.
50. Kutasovic JR, McCart Reed AE, Males R, Sim S, Saunus JM, Dalley A, et al. Breast cancer metastasis to gynaecological organs: a clinico-pathological and molecular profiling study. The Journal of Pathology: Clinical Research. 2019;5:25-39.
51. Nili F, Tavakoli M, Mood NI, Saffar H, Sarmadi S. Napsin-A Expression, a Reliable Immunohistochemical Marker for Diagnosis of Ovarian and Endometrial Clear Cell Carcinomas. Iranian journal of pathology. 2020;15:81.
52. Amanullah NA, Poothiode U, Vilasiniamma L. Expression of p53 in epithelial ovarian tumors. Indian Journal of Pathology and Microbiology. 2020;63:235.

53. Nayak S, Kumari P, Agrawal KC. Immunohistochemical expression of p53 in serous carcinoma of ovary and its correlation with clinicopathological parameters. Indian Journal of Pathology and Oncology. 2020;7:33-8.
54. Rambau PF, Köbel M, Tilley D, Mremi A, Lukande R, Muller W. Ovarian cancer: diagnostic accuracy and tumor types distribution in East Africa compared to North America. Diagnostic Pathology. 2020;15:1-1.
55. Köbel M, Rahimi K, Rambau PF, Naugler C, Le Page C, Meunier L, et al. An immunohistochemical algorithm for ovarian carcinoma typing. International Journal of Gynecological Pathology. 2016;35:430.
56. Ho CM. Pattern of ovarian tumours among Malaysian women at General Hospital~ Kuala Lumpur. Med. J. Malaysia. 1992;47.
57. Batool A, Rathore Z, Jahangir F, Javeed S, Nasir S, Chughtai AS. Histopathological Spectrum of Ovarian Neoplasms: A Single-Center Study. Cureus. 2022;14.
58. ModePalli N, VeNugoPal SB. Clinicopathological study of surface epithelial tumours of the ovary: An institutional study. Journal of clinical and diagnostic research: JCDR. 2016;10:EC01.
59. Goel A, Rao NM, Santhi V, Grandhi B. Immunohistochemical characterization of normal ovary and common epithelial ovarian neoplasm with a monoclonal antibody to cytokeratin and vimentin. Iranian journal of pathology. 2018;13:23.
60. Kaushik N, Rani D, Prakash S, Singh R, Kumar L. Histomorphological Features of Ovarian Neoplasms and Expression of p53 and WT1 in Surface Epithelial Tumours: A Cross-sectional Study. Journal of Clinical & Diagnostic Research. 2022;16.
61. Sallum LF, Andrade L, Ramalho S, Ferracini AC, de Andrade Natal R, Brito AB, et al. WT1, p53 and p16 expression in the diagnosis of low-and high-grade serous ovarian carcinomas and their relation to prognosis. Oncotarget. 2018;9:15818.

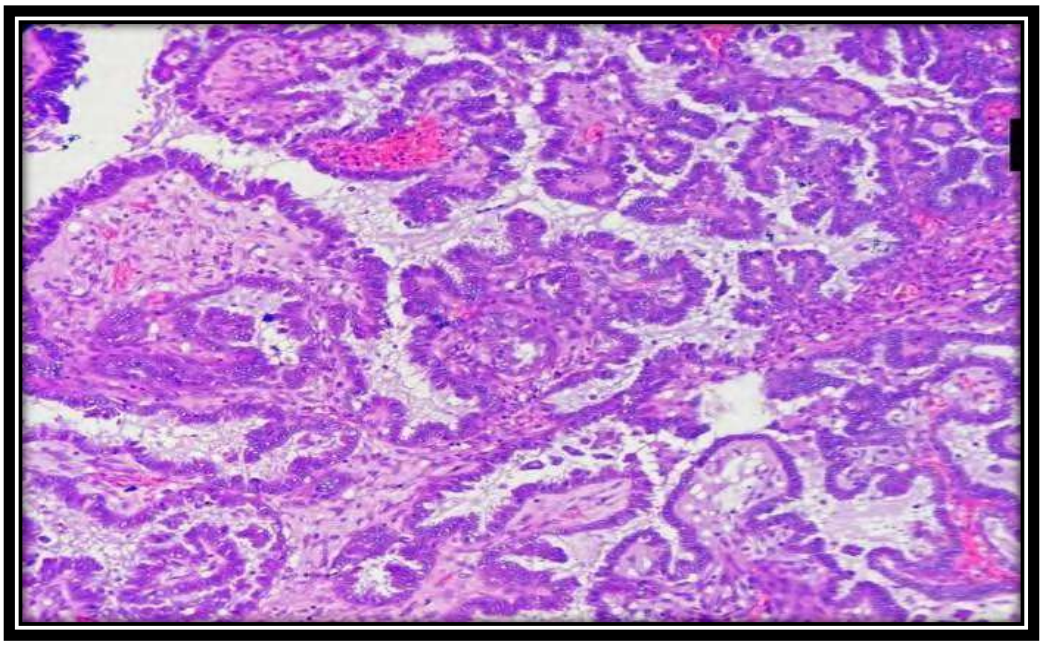
62. Köbel M, Bak J, Bertelsen BI, Carpen O, Grove A, Hansen ES, et al. Ovarian carcinoma histotype determination is highly reproducible, and is improved through the use of immunohistochemistry. Histopathology. 2014;64:1004-13.
63. Chatterjee A, Sen S, Clinicopathological study of epithelial neoplasms of ovary with special reference to the expression of P53 and Her2/neu in epithelial carcinoma. Indian J Pathol Oncol 2022;9:52-59.
64. Babaier A, Ghatage P. Mucinous cancer of the ovary: overview and current status. Diagnostics. 2020;10:52.
65. Vang R, Gown AM, Barry TS, Wheeler DT, Yemelyanova A, Seidman JD, et al. Immunohistochemical expression of CDX2 in primary ovarian mucinous tumors and metastatic mucinous carcinomas involving the ovary: comparison with CK20 and correlation with coordinate expression of CK7. Modern Pathology. 2006;19:1421-8.
66. Atla B, Sarkar RN, Rasaputra M. Clinicopathological and IHC study (estrogen receptors, progesterone receptor, HER2/NEU) in malignant ovarian tumors. Int J Res Med Sci. 2016;4:1068-73.
67. Skirnisdottir I, Bjersand K, Åkerud H, Seidal T. Napsin A as a marker of clear cell ovarian carcinoma. BMC cancer. 2013;13:1-2.
68. Iwamoto M, Nakatani Y, Fugo K, Kishimoto T, Kiyokawa T. Napsin A is frequently expressed in clear cell carcinoma of the ovary and endometrium. Human Pathology. 2015;46:957-62.
69. Hollis RL, Croy I, Churchman M, Bartos C, Rye T, Gourley C, Herrington CS. Ovarian carcinosarcoma is a distinct form of ovarian cancer with poorer survival compared to tubo-ovarian high-grade serous carcinoma. British Journal of Cancer. 2022;127:1034-42.
70. Lee Y, Na K, Woo HY, Kim HS. Alveolar Soft Part Sarcoma of the Uterus:Clinicopathological and Molecular Characteristics. Diagnostics. 2022;12:1102.
71. McFarland M, Quick CM, McCluggage WG. Hormone receptor-negative, thyroid transcription factor 1-positive uterine and

ovarian adenocarcinomas: report of a series of mesonephric-like adenocarcinomas. Histopathology. 2016;68:1013-20.

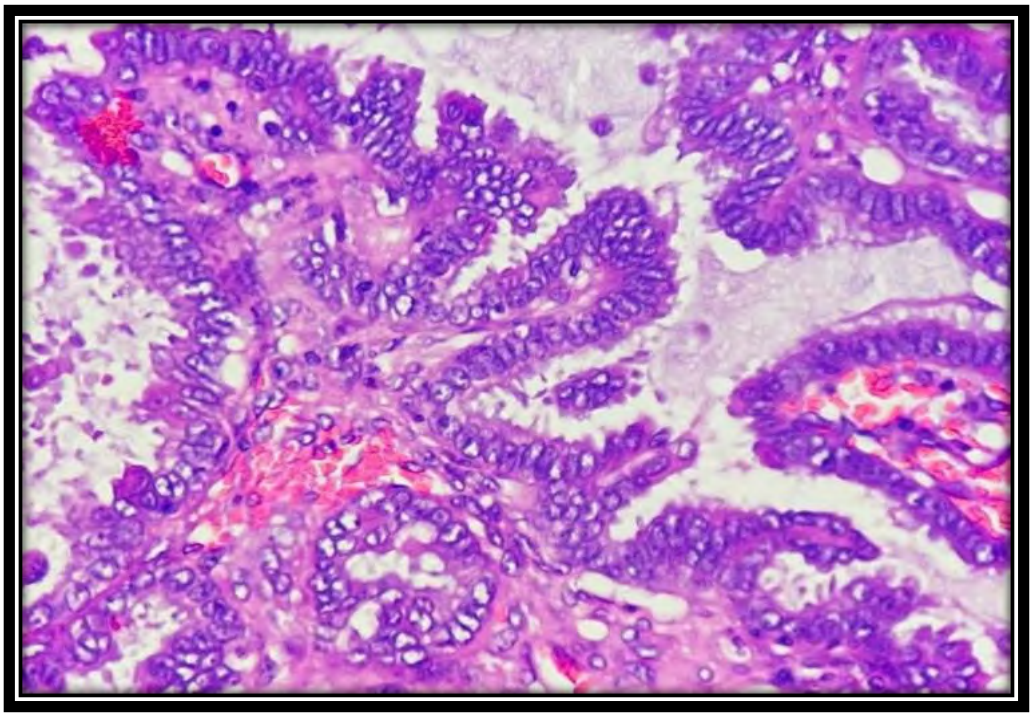
72. Nagamine M, Mikami Y. Ovarian seromucinoustumors: pathogenesis, morphologic spectrum, and clinical issues. Diagnostics. 2020;10:77.
73. Roma AA, Masand RP. Different staining patterns of ovarian Brenner tumor and the associated mucinous tumor. Annals of diagnostic pathology. 2015;19:29-32.
74. Hauptmann S, Friedrich K, Redline R, Avril S. Ovarian borderline tumors in the 2014 WHO classification: evolving concepts and diagnostic criteria. Virchowsarchiv. 2017;470:125-42.
75. Fayek IS, Amira G, Habashy NF, Attia MA. A Retrospective Study of Ovarian Sex Cord Stromal Tumors at the Egyptian National Cancer Institute. Journal of Cancer Therapy. 2019;10:920.
76. Haroon S, Zia A, Idrees R, Memon A, Fatima S, Kayani N. Clinicopathological spectrum of ovarian sex cord-stromal tumors; 20 years' retrospective study in a developing country. Journal of ovarian research. 2013;6:1-8.
77. Guleria P, Kumar L, Kumar S, Bhatla N, Ray R, Singhal S, et al. A clinicopathological study of granulosa cell tumors of the ovary: Can morphology predict prognosis?. Indian Journal of Pathology and Microbiology. 2020;63:53.
78. Costa MJ, Ames PF, Walls J, Roth LM. Inhibin immunohistochemistry applied to ovarian neoplasms: a novel, effective, diagnostic tool. Human pathology. 1997 ;28:1247-54.
79. Ye Y, Lv C, Xu S, Chen Y, Qian R, Wang P, et al. Juvenile Granulosa Cell Tumors of the Ovary: A Clinicopathologic Study of 7 Cases and a Review of the Literature. American Journal of Clinical Pathology. 2020;154:635-44.
80. Chougule A, Garg R. SMA-Positive fibroma with an intramural endometriotic cyst mimicking ovarian leiomyoma. Applied Immunohistochemistry & Molecular Morphology. 2017;25:e38-9.

81. Kommoss F, Oliva E, Bhan AK, Young RH, Scully RE. Inhibin expression in ovarian tumors and tumor-like lesions: an immunohistochemical study. Mod Pathol. 1998;11:656-64.
82. Zhao C, Bratthauer GL, Barner R, Vang R. Diagnostic utility of WT1 immunostaining in ovarian sertoli cell tumor. The American journal of surgical pathology. 2007;31:1378-86.
83. Yada-Hashimoto N, Yamamoto T, Kamiura S, Seino H, Ohira H, Sawai K, et al. Metastatic ovarian tumors: a review of 64 cases. Gynecologic oncology. 2003;89:314-7.
84. Khunamornpong S, Suprasert P, Chiangmai WN, Siriaunkgul S. Metastatic tumors to the ovaries: a study of 170 cases in northern Thailand. International Journal of Gynecologic Cancer. 2006;16.
85. Lee SJ, Bae JH, Lee AW, Tong SY, Park YG, Park JS. Clinical characteristics of metastatic tumors to the ovaries. Journal of Korean medical science. 2009 ;24:114-9.
86. Goldstein NS, Uzieblo A. WT1 immunoreactivity in uterine papillary serous carcinomas is different from ovarian serous carcinomas. American journal of clinical pathology. 2002;117:541-5.
87. Acs G, Pasha T, Zhang PJ. WT1 is differentially expressed in serous, endometrioid, clear cell, and mucinous carcinomas of the peritoneum, fallopian tube, ovary, and endometrium. International Journal of Gynecological Pathology. 2004;23:110-8.
88. Egan JA, Ionescu MC, Eapen E, Jones JG, Marshall DS. Differential expression of WT1 and p53 in serous and endometrioid carcinomas of the endometrium. International journal of gynecological pathology. 2004;23:119-22.
89. Wu X, Li F, Iroegbu CD, Fan C, Song G. A Rare Case of Cardiac Metastatic Uterine Intravenous Leiomyomatosis. Frontiers in Cardiovascular Medicine. 2022;9.
90. Kubeček O, Laco J, Špaček J, Petera J, Kopecký J, Kubečková A, et al. The pathogenesis, diagnosis, and management of metastatic tumors to the ovary: a comprehensive review. Clinical & experimental metastasis. 2017;34:295-307.

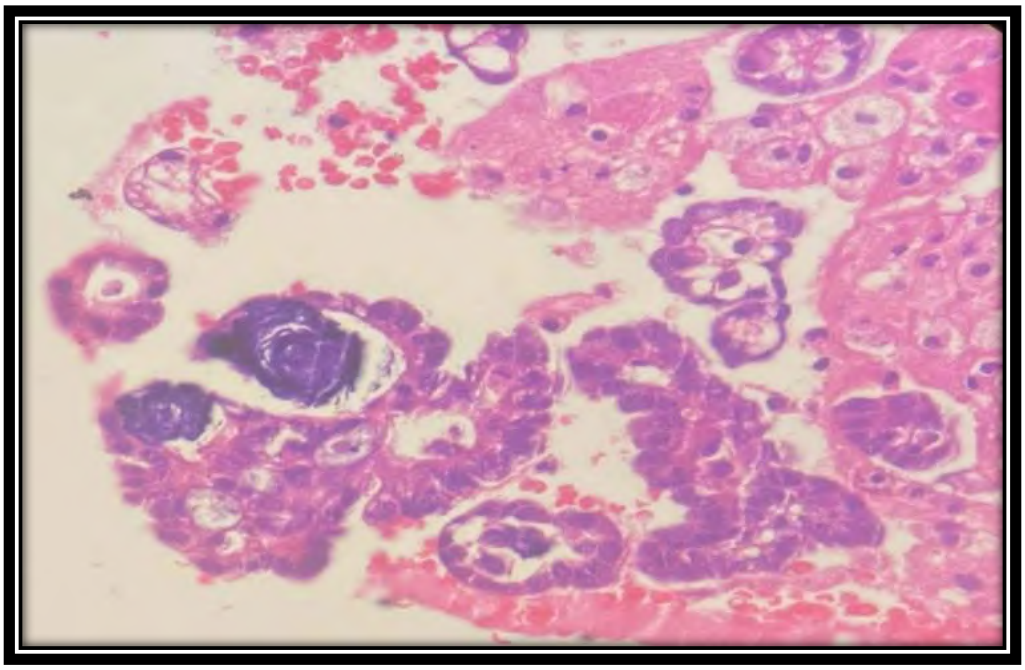
91. Gică N, Peltecu G, Chirculescu R, Gică C, Stoicea MC, Serbanica AN, et al. Ovarian Germ Cell Tumors: Pictorial Essay. Diagnostics. 2022 ;12:2050.
92. Lifschitz-Mercer B, Walt H, Kushnir I, Jacob N, Diener PA, Moll R, et al. Differentiation potential of ovarian dysgerminoma: an immunohistochemical study of 15 cases. Human pathology. 1995;26:62-6.
93. Teng LH, Lu DH, Xu QZ, Fu YJ, Yang H, He ZL. Expression and diagnostic significance of OCT4, CD117 and CD30 in germ cell tumors. Zhonghuabing li xue za zhi Chinese journal of pathology. 2005;34:711-5.
94. Chaudhary RK, Kher A, Bobhate SK, Grover S. Alpha-fetoprotein in germ cell tumors. An immunohistochemical study. Indian Journal of Pathology & Microbiology. 1989;32:167-73.
95. Zynger DL, McCallum JC, Luan C, Chou PM, Yang XJ. Glypican 3 has a higher sensitivity than alpha-fetoprotein for testicular and ovarian yolk sac tumour: immunohistochemical investigation with analysis of histological growth patterns. Histopathology. 2010;56:750-7.
96. Lerwill MF, Sung R, Oliva E, Prat J, Young RH. Smooth muscle tumors of the ovary: a clinicopathologic study of 54 cases emphasizing prognostic criteria, histologic variants, and differential diagnosis. The American journal of surgical pathology. 2004;28:1436-51.



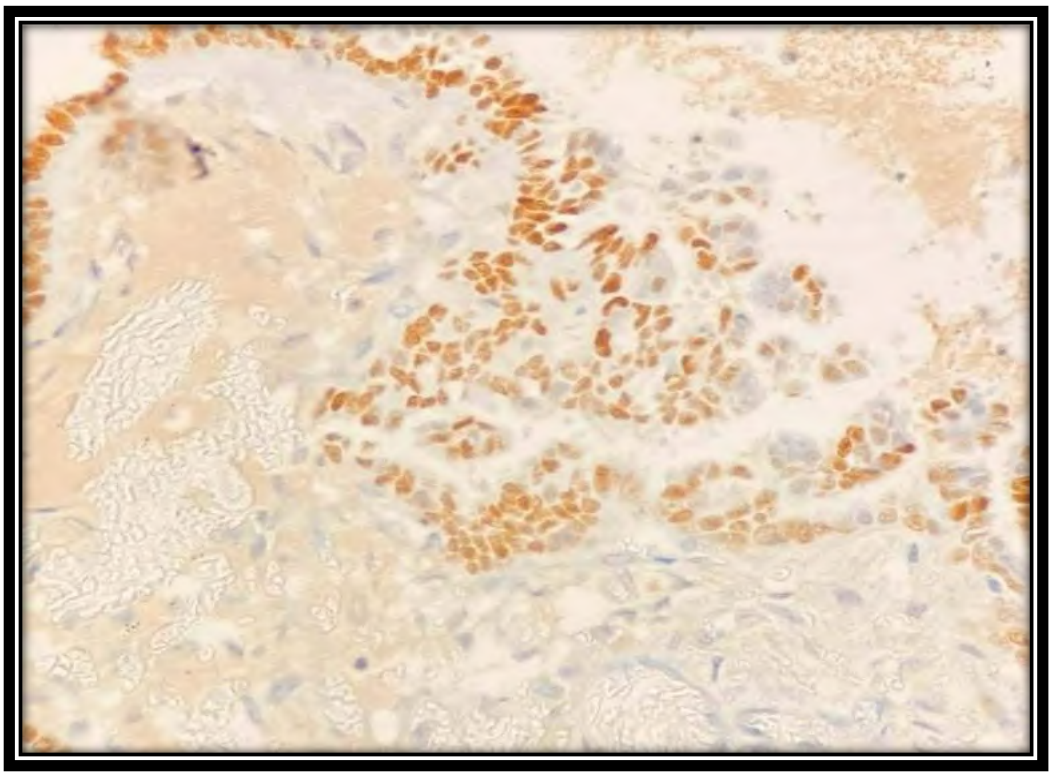
Picture 1- Photomicrograph of low grade serous carcinoma showing arborising papillae lined by tumour cells (H&E, 100X)



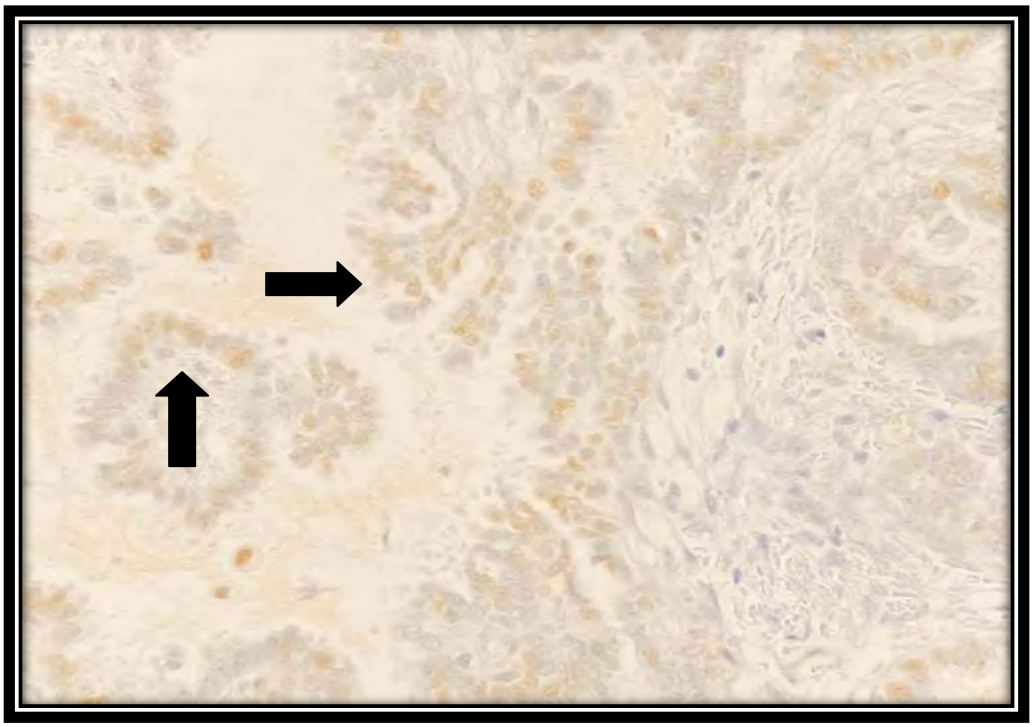
Picture 2- Photomicrograph of low grade serous carcinoma showing mild to moderate nuclear atypia (< 3 fold variability in nuclear size), conspicuous nucleoli (H&E, 400X)



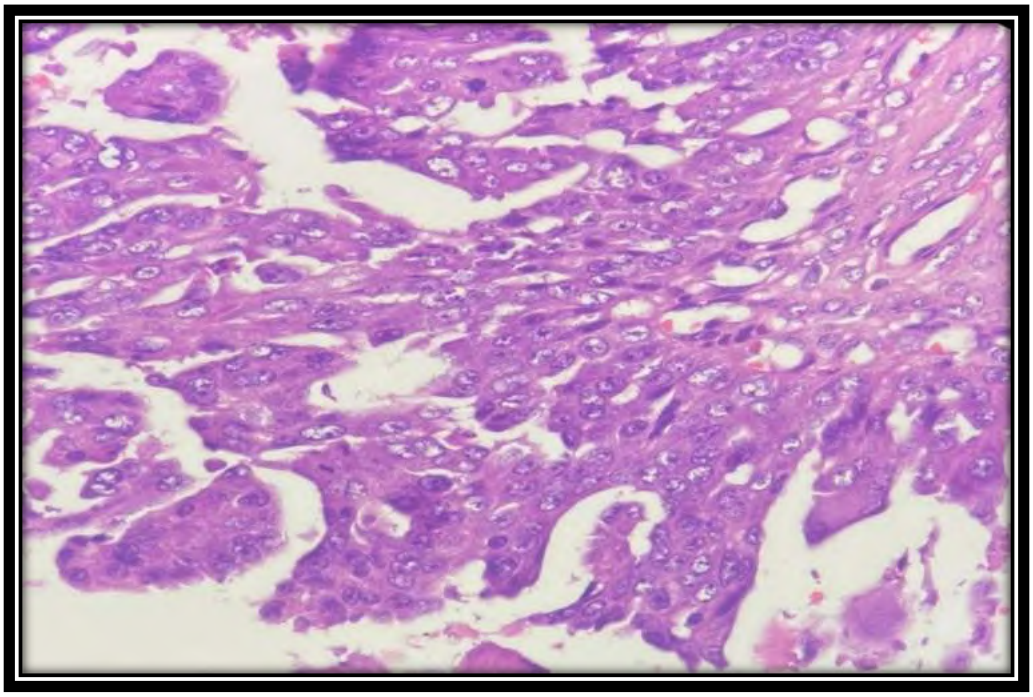
Picture 3 - Photomicrograph of low grade serous carcinoma showing lamellated psammoma bodies (H&E,400X)



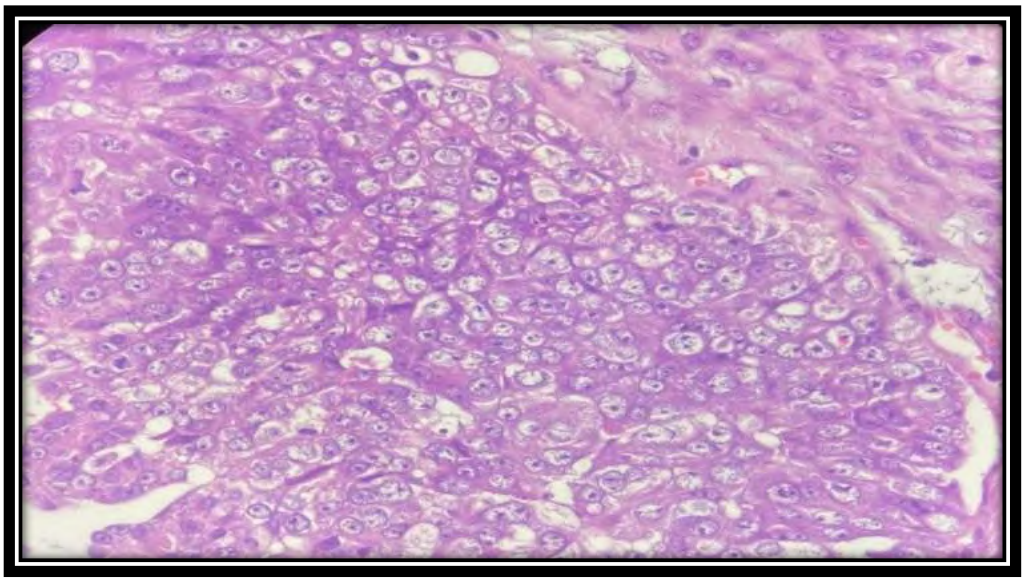
Picture 4 - Photomicrograph of low grade serous carcinoma showing diffuse nuclear positivity of WT1 (IHC, 400X)



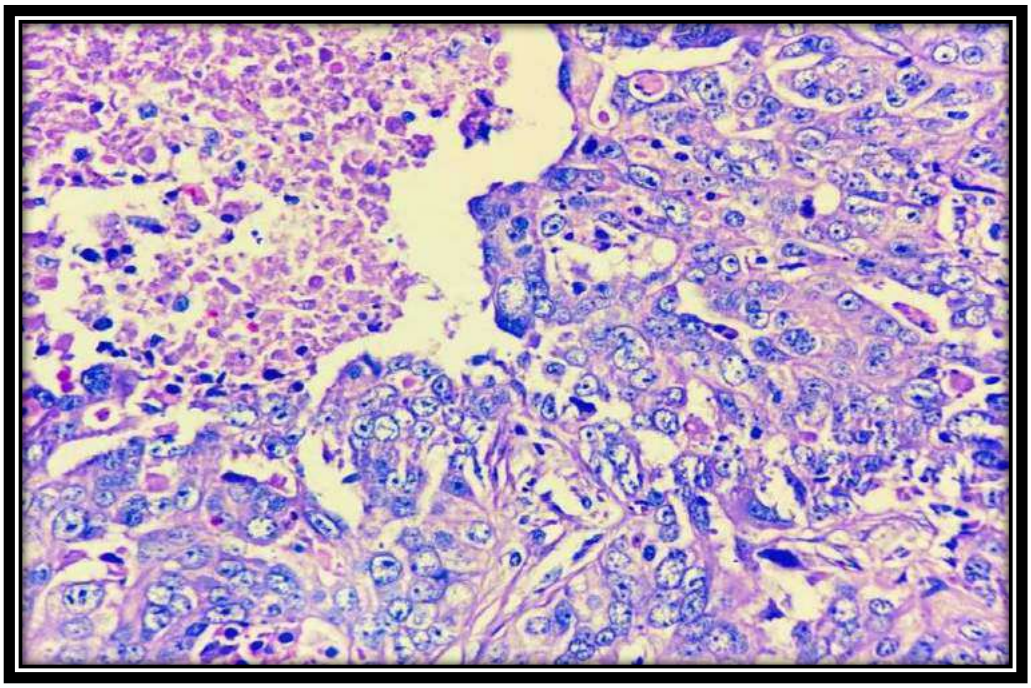
Picture 5- Photomicrograph of low grade serous carcinoma showing wild type positivity of p53 (Arrow) (IHC, 400X)



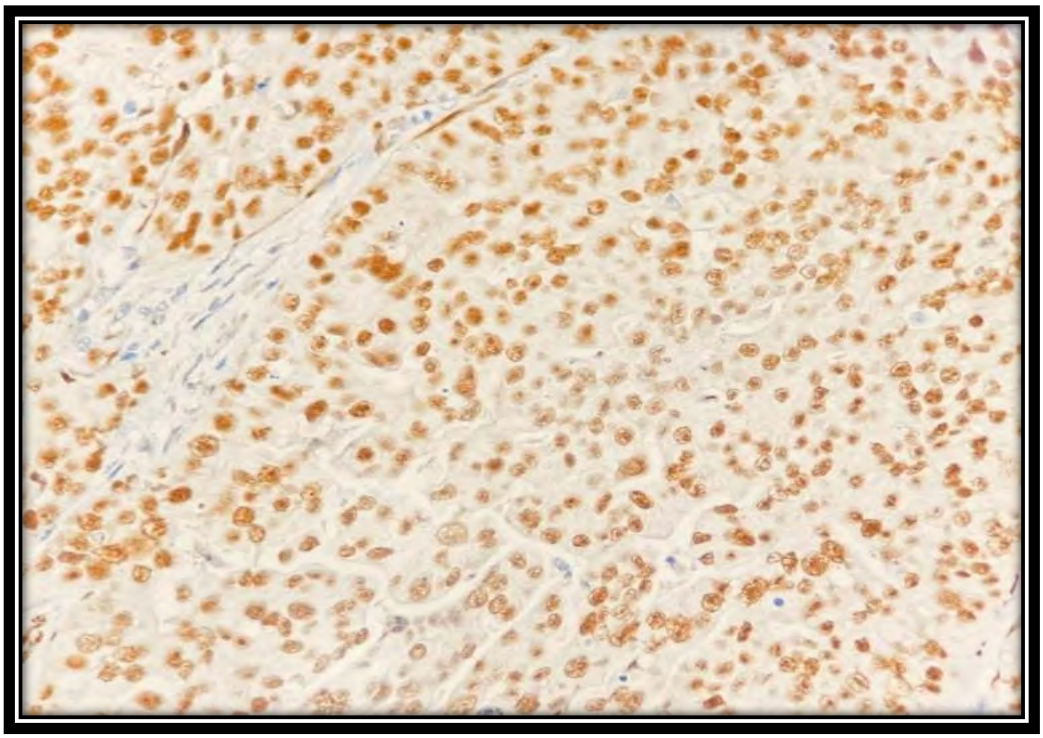
Picture 6 - Photomicrograph of high grade serous carcinoma showing tumour arranged in glandular configuration and nests (H&E, 100X)



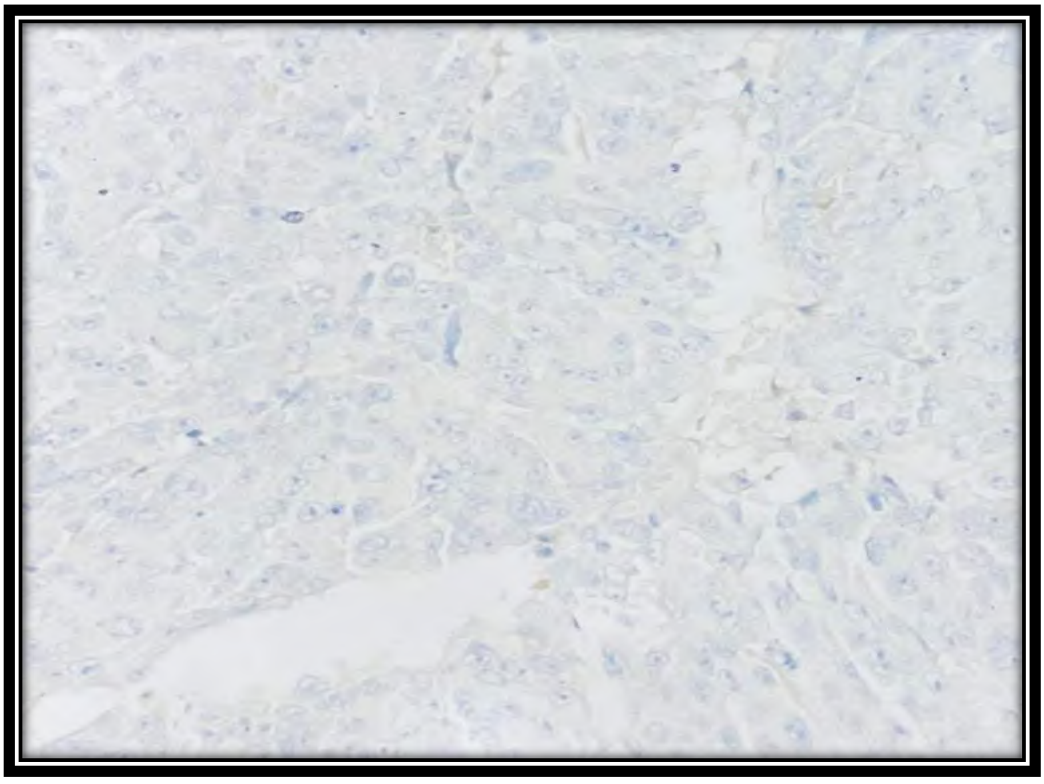
Picture 7- Photomicrograph of high grade serous carcinoma showing tumour cells having pleomorphic vesicular nuclei, prominent nucleoli and moderate cytoplasm (H&E, 400X)



Picture 8 - Photomicrograph of high grade serous carcinoma showing tumour cells arranged in sheets with marked nuclear pleomorphism (nuclear variability >3 fold), prominent nucleoli and foci of necrosis (H&E, 400X)

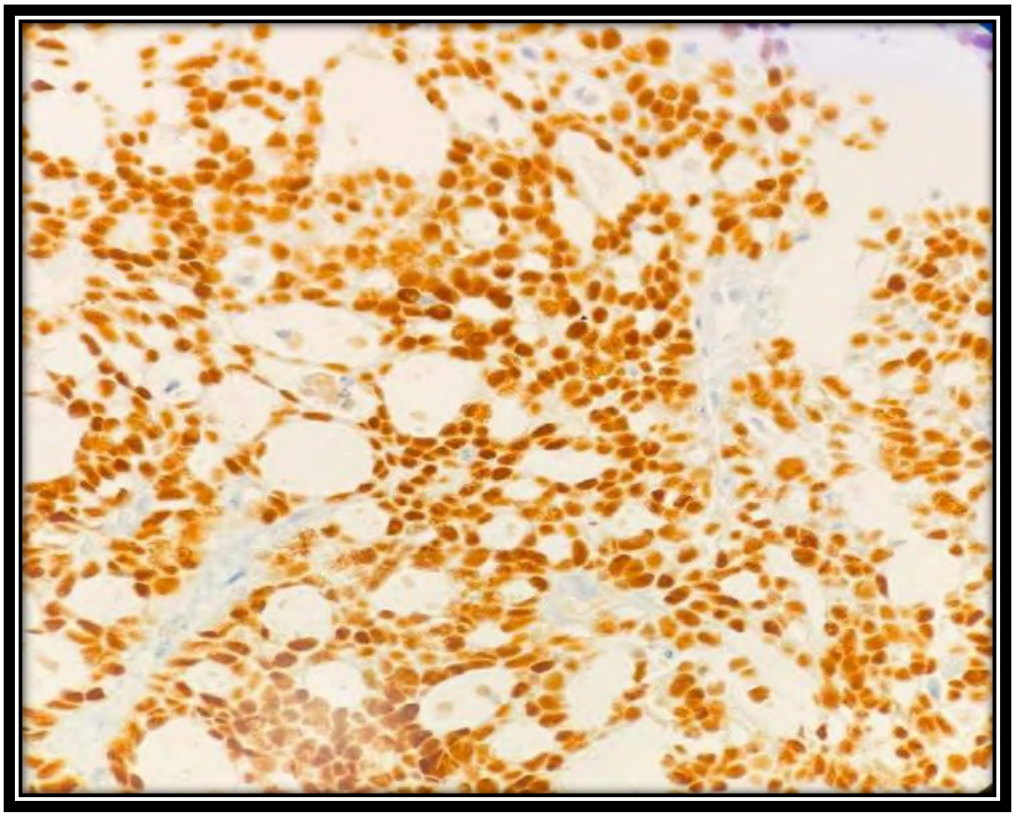


Picture 9 - Photomicrograph of high grade serous carcinoma showing diffuse nuclear positivity of WT1 (IHC, 400X)

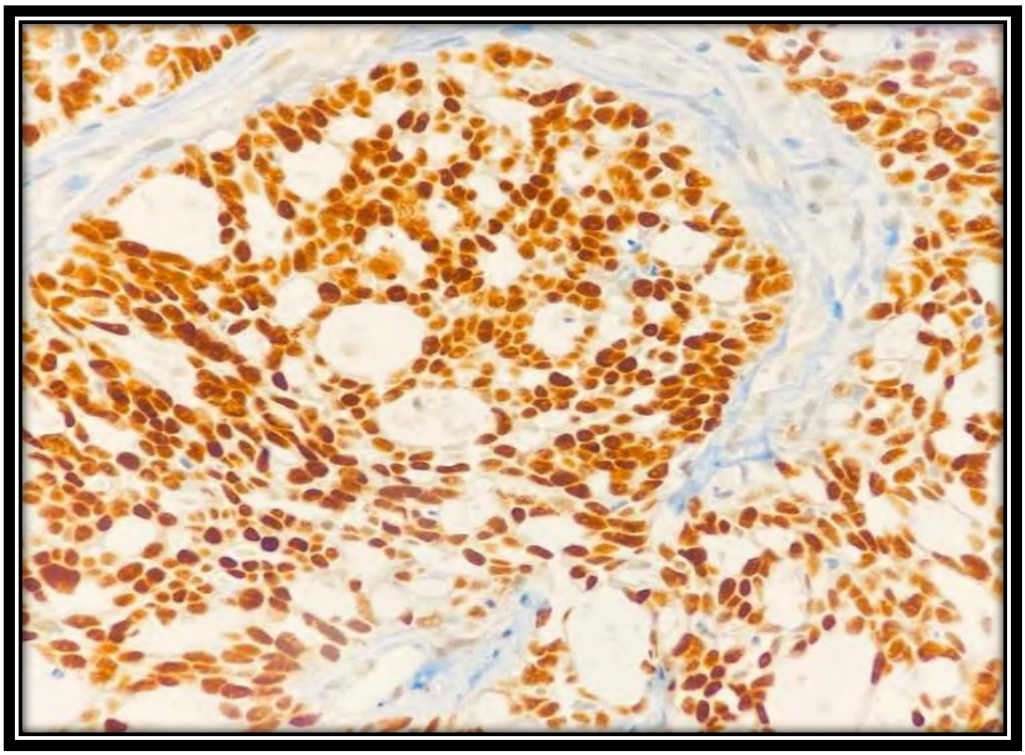


Picture 10 - Photomicrograph of high grade serous carcinoma showing null type p53 (IHC, 400X)

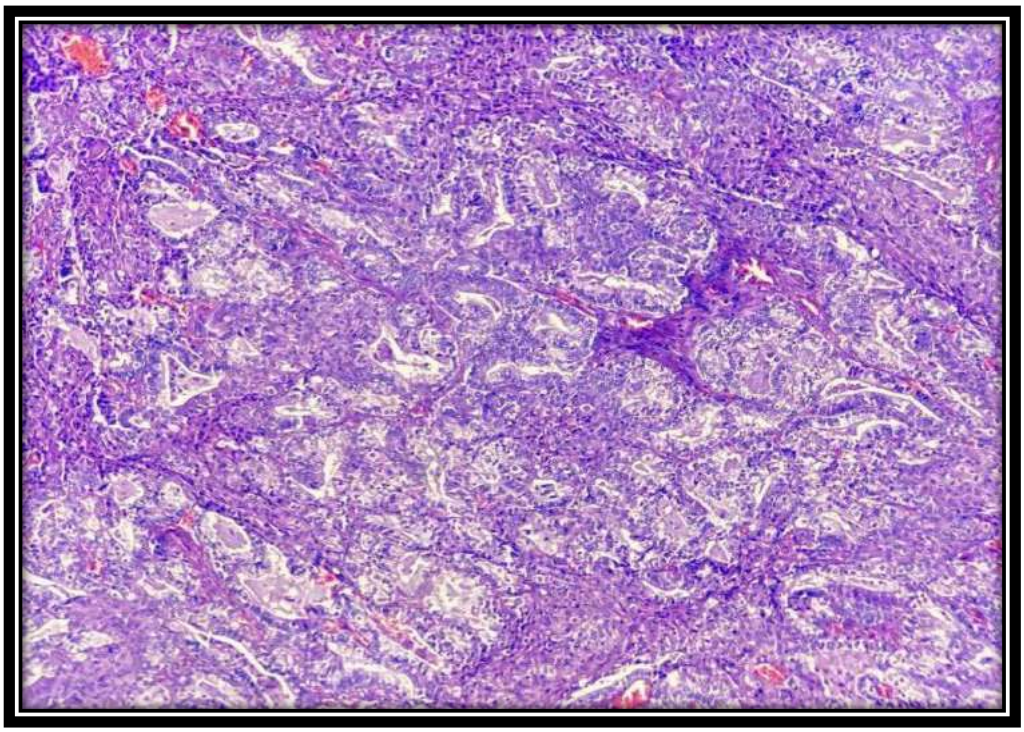
Picture 11- Photomicrograph of high grade serous carcinoma showing diffuse nuclear/cytoplasmic positivity of p16 (IHC, 400X)



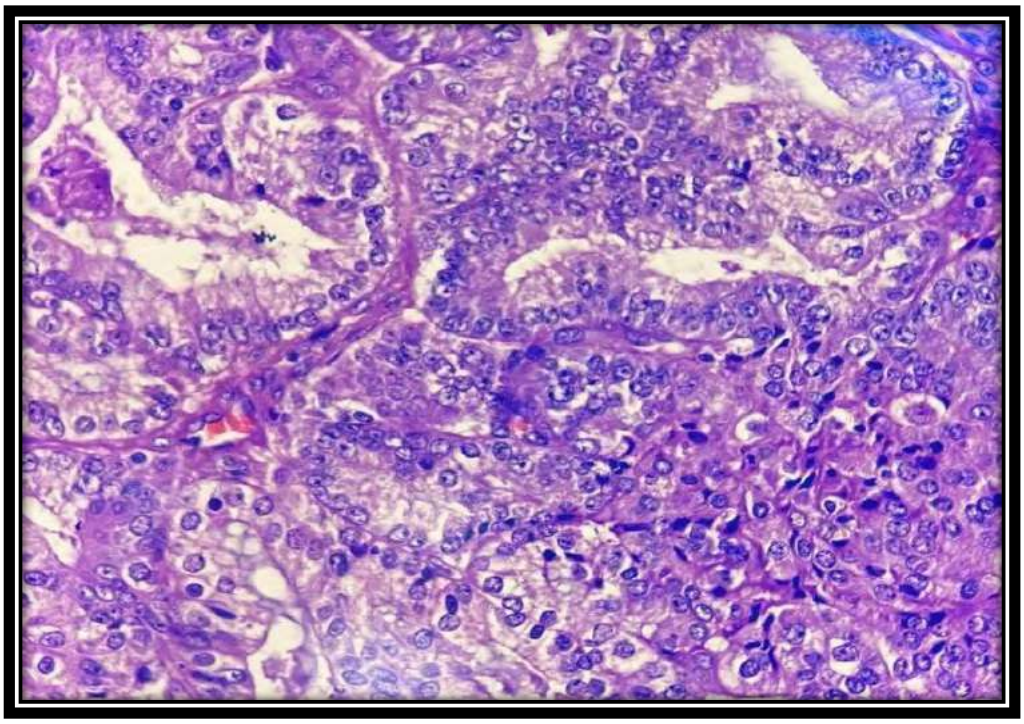
Picture 12- Photomicrograph of high grade serous carcinoma showing diffuse nuclear positivity of WT1 (IHC, 400X)



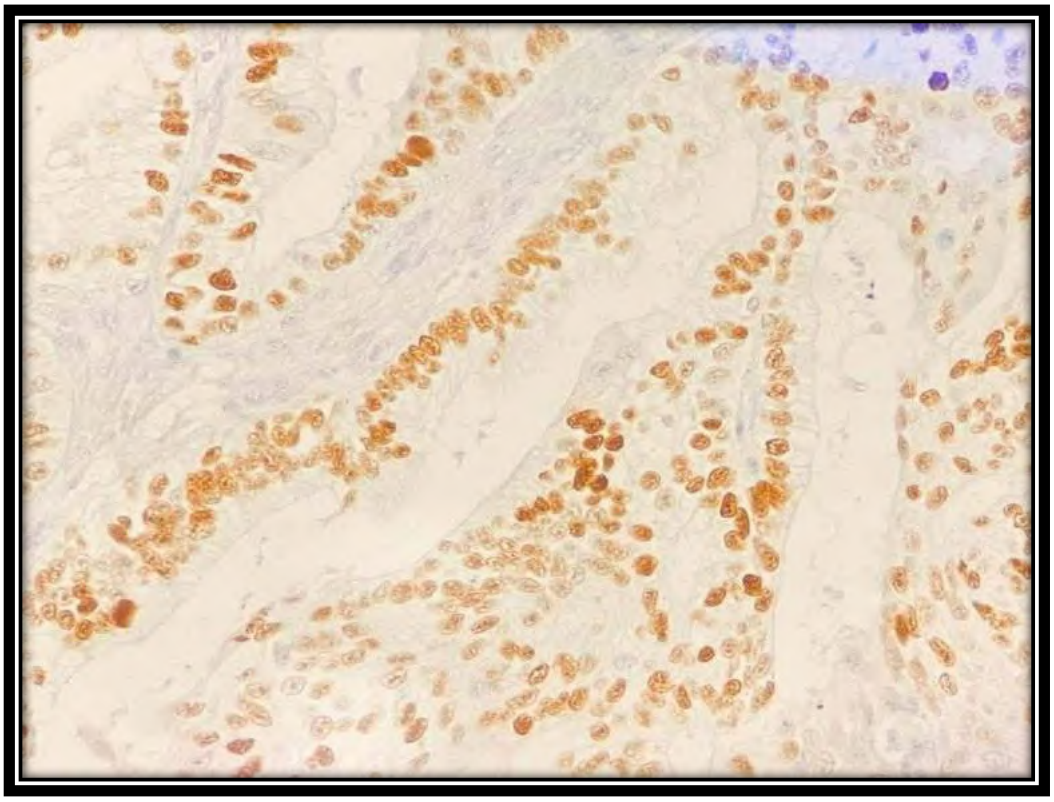
Picture 13- Photomicrograph of high grade serous carcinoma showing diffuse nuclear positivity of p53 (IHC, 400X)



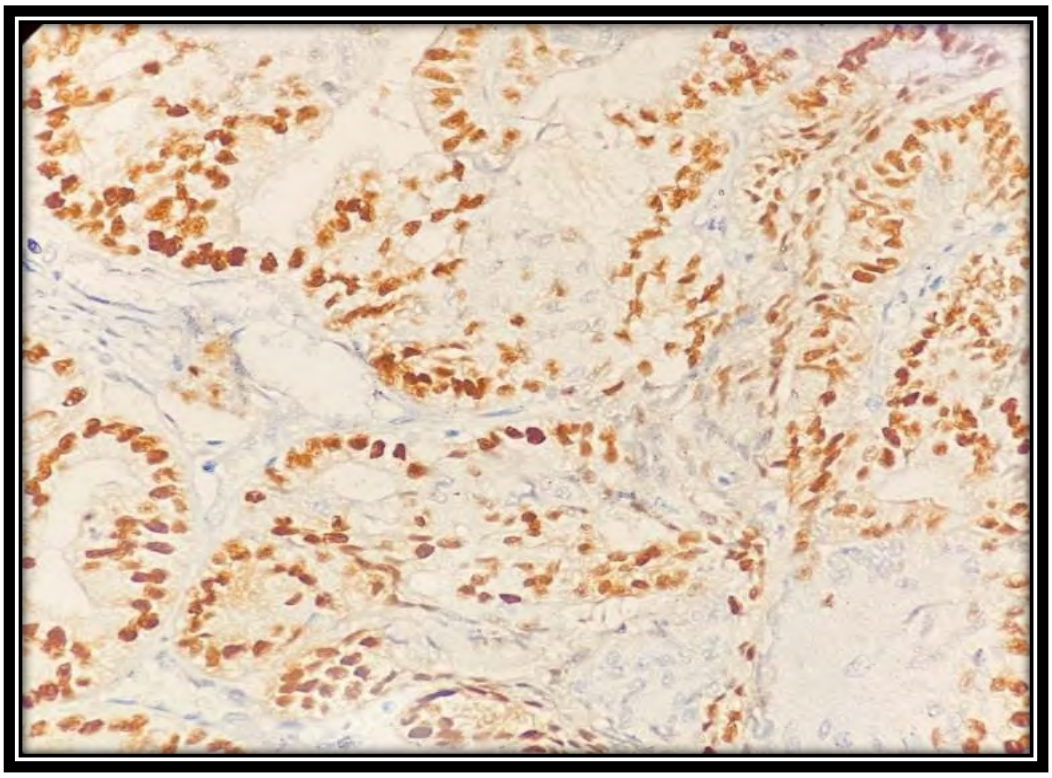
Picture 14- Photomicrograph of endometrioid carcinoma showing tumour arranged in back to back glandular arrangement lined by tumour cells with well defined luminal margins. (H&E,100X)



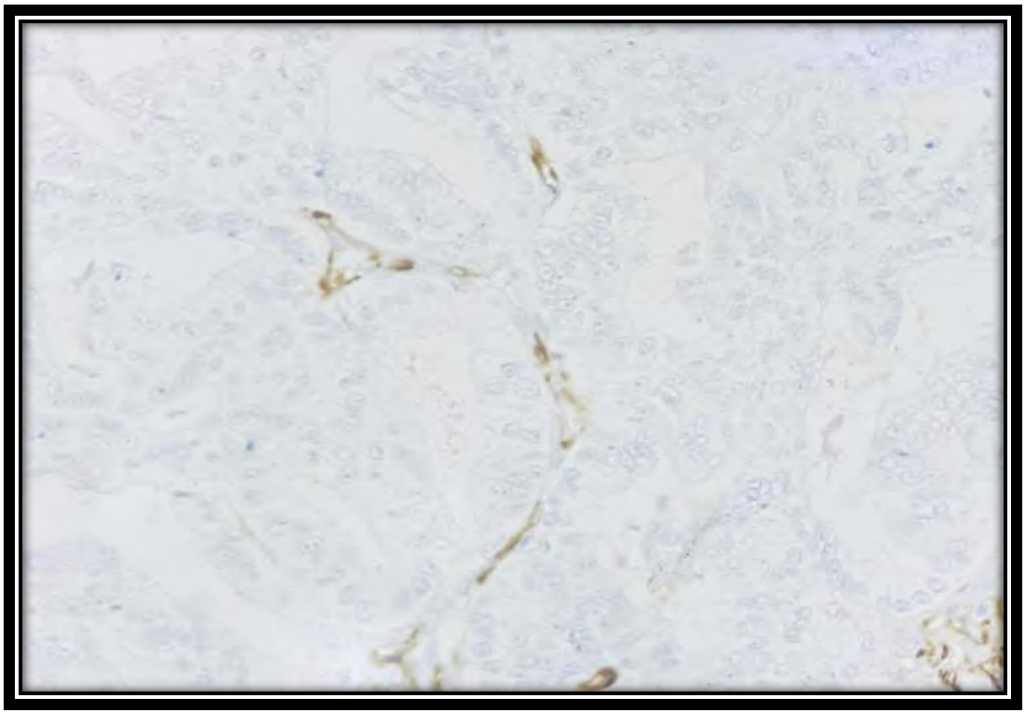
Picture 15 - Photomicrograph of endometrioid carcinoma showing tumour having vesicular nuclei and moderate cytoplasm. (H&E,400X)



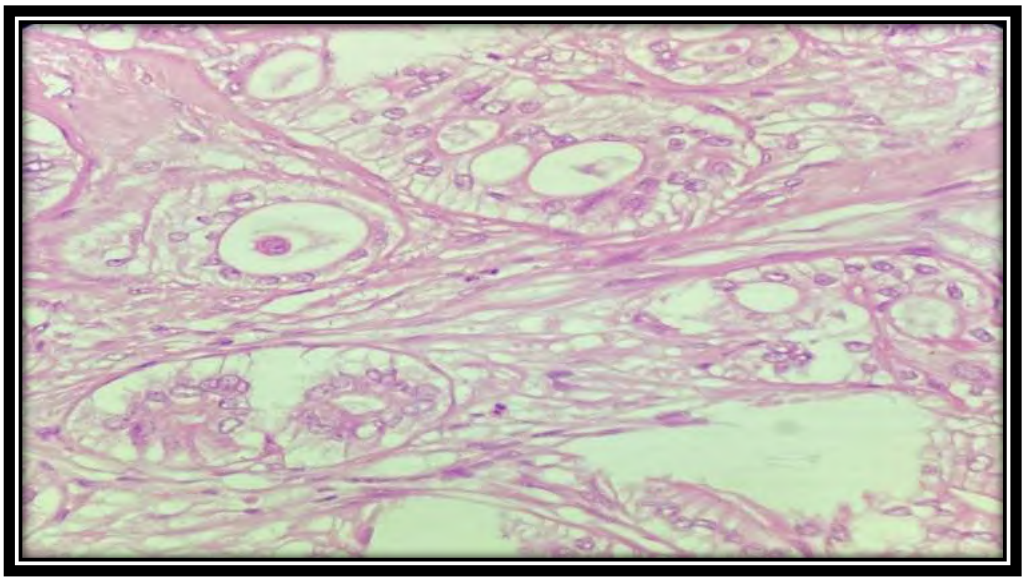
Picture 16 - Photomicrograph showing diffuse nuclear ER positivity in endometrioid carcinoma (IHC, 400X)



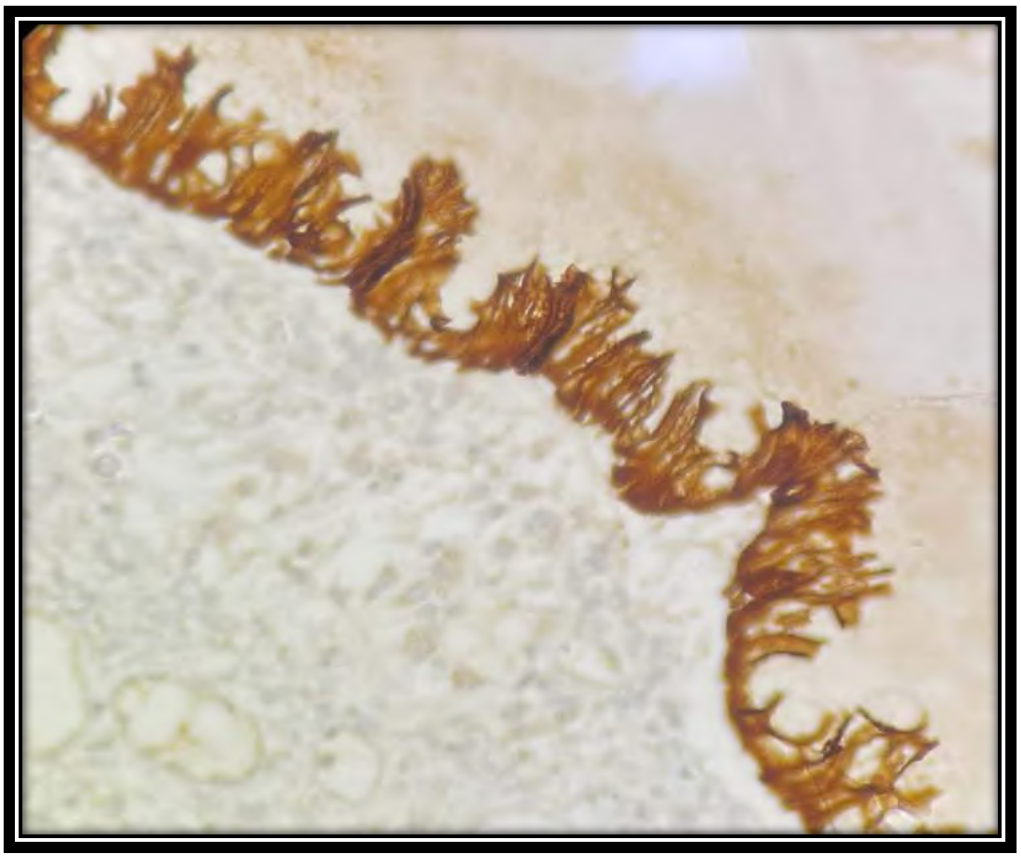
Picture 17 - Photomicrograph showing diffuse nuclear PR positivity in endometrioid carcinoma (IHC, 400X)



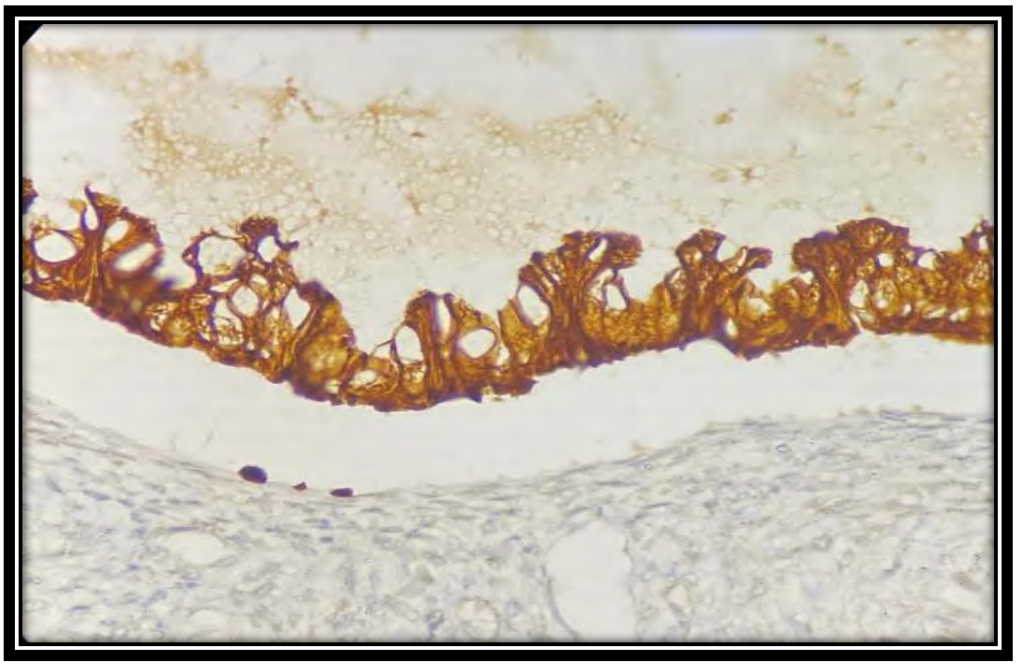
Picture 18 - Photomicrograph of endometrioid carcinoma showing WT1 negativity (IHC, 400X)



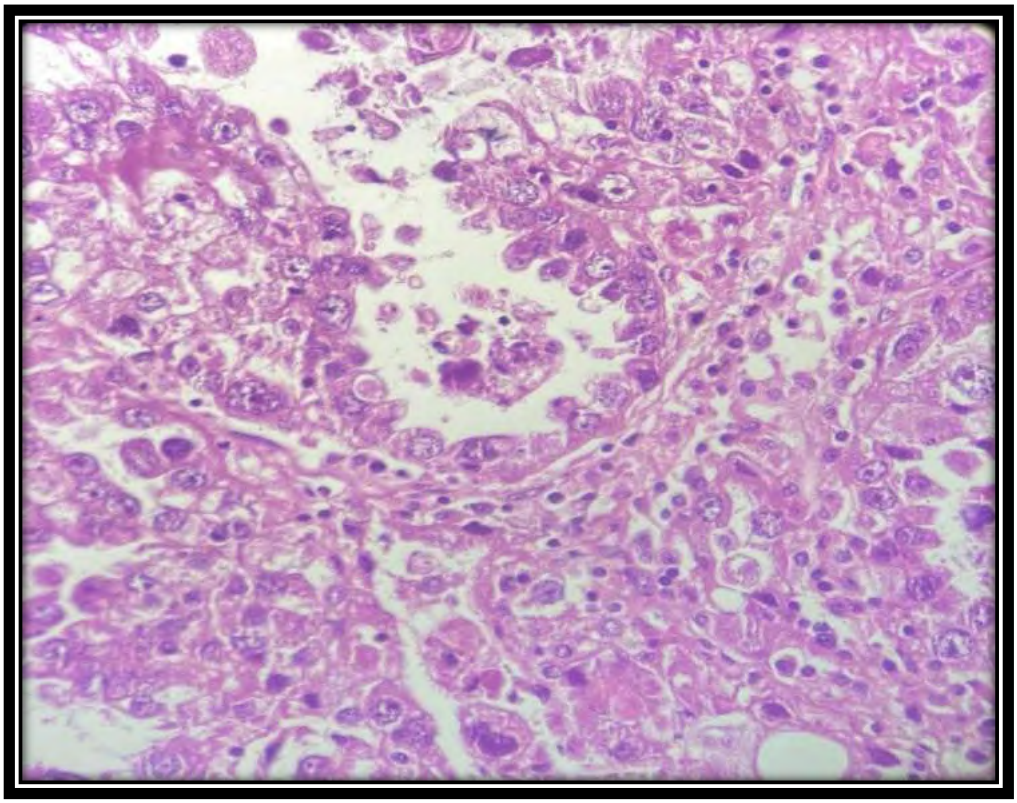
Picture 19- Photomicrograph of mucinous carcinoma showing tumour arranged in glandular configuration lined by mucinous cells (H&E,400X)



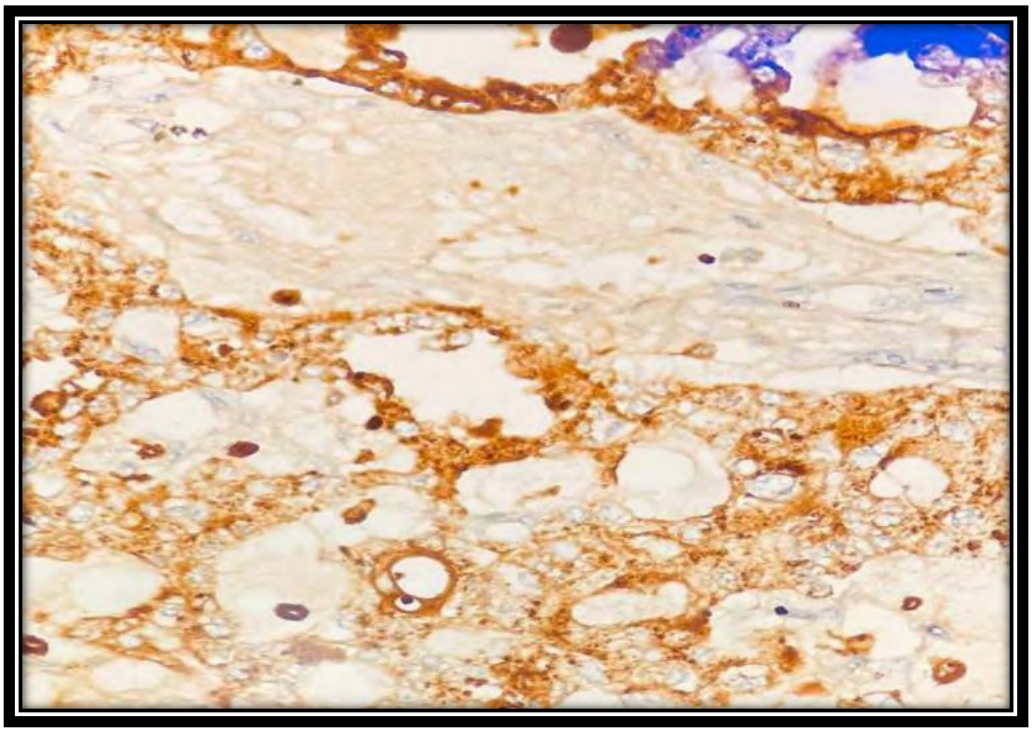
Picture 20 - Photomicrograph of mucinous carcinoma showing cytoplasmic CK20 positivity (IHC,400X)



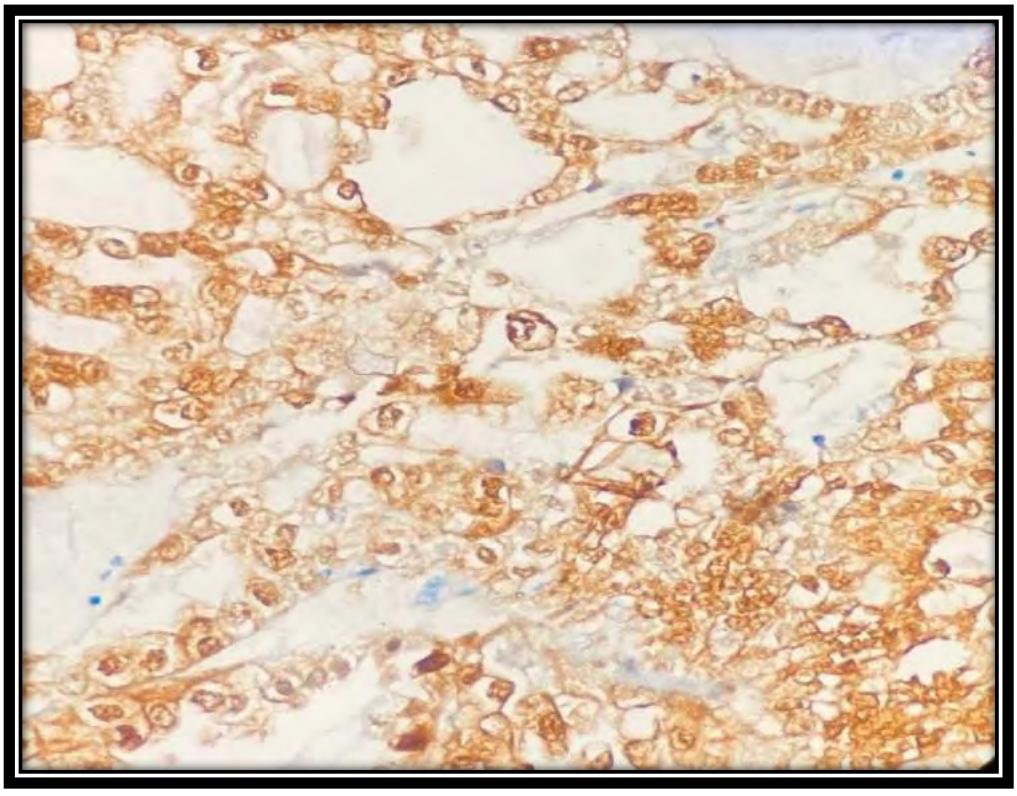
Picture 21 - Photomicrograph of mucinous carcinoma showing cytoplasmic CK7 positivity (IHC,400X)



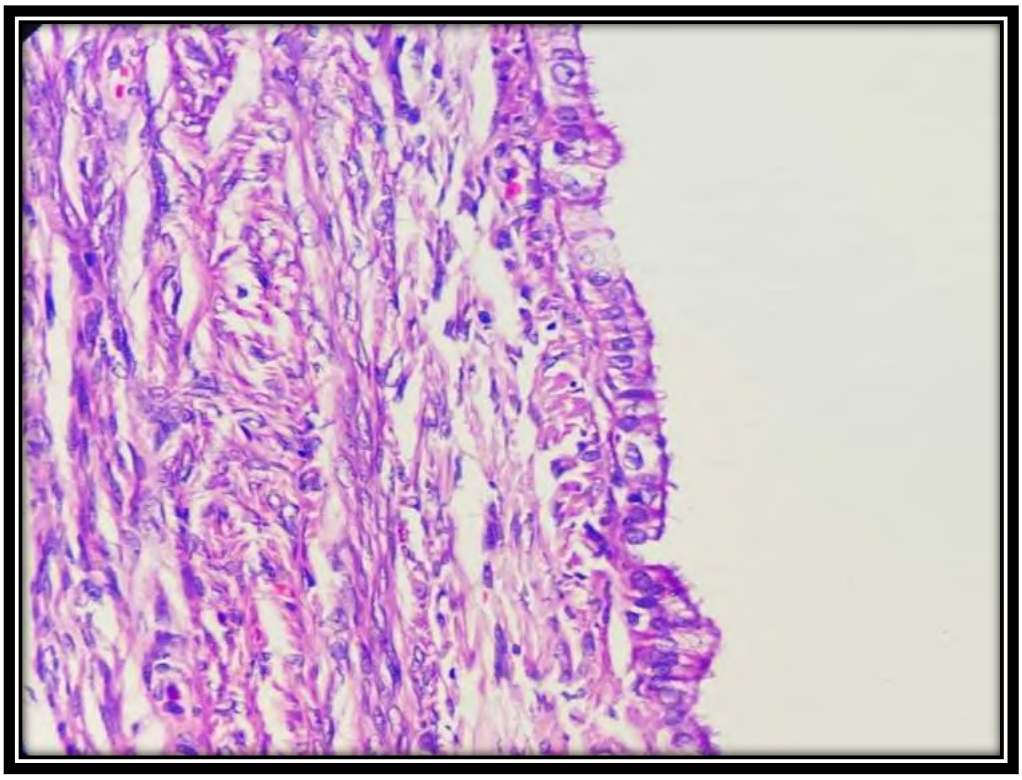
Picture 22 - Photomicrograph of clear cell carcinoma showing tumour cells having clear cytoplasm with round to angulated vesicular nuclei and hobnailing (H&E, 400X)



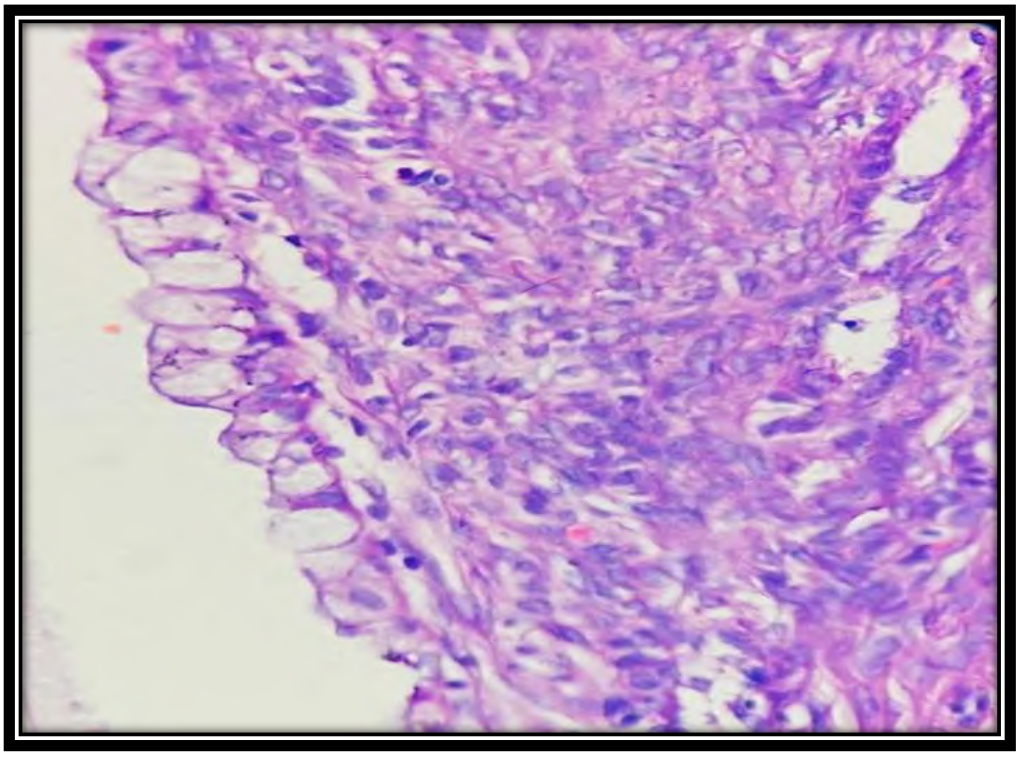
Picture 23 - Photomicrograph of clear cell carcinoma showing diffuse cytoplasmic positivity of Napsin A (IHC, 400X)



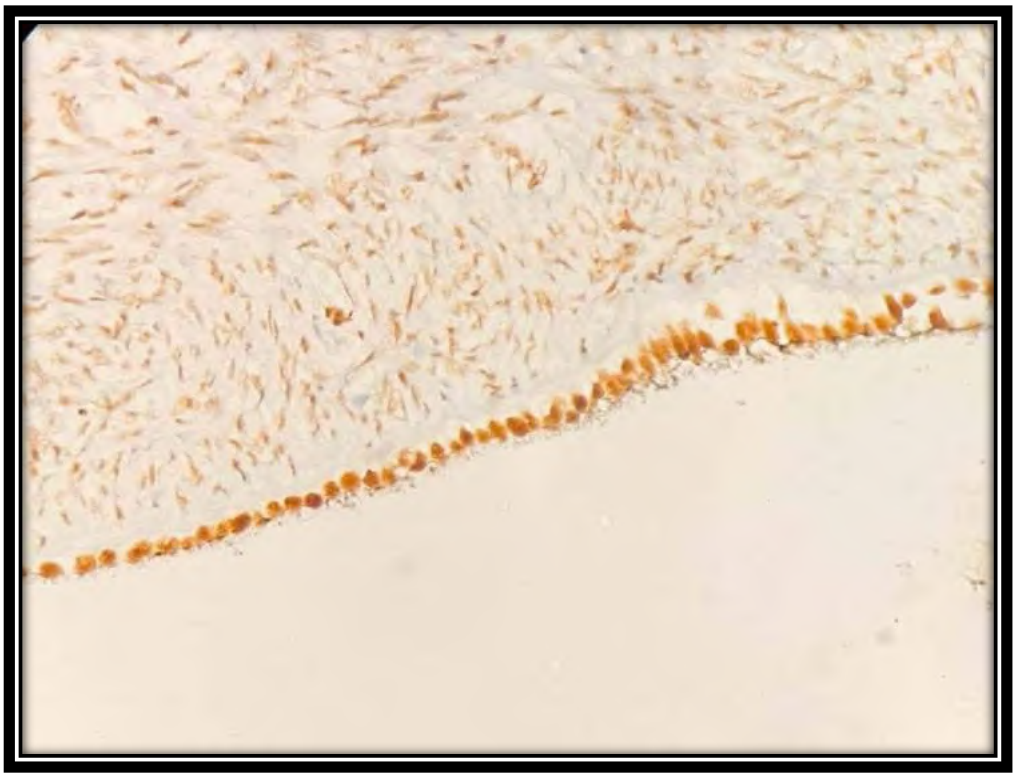
Picture 24 - Photomicrograph of clear cell carcinoma showing diffuse nuclear/cytoplasmic positivity of p16 (IHC, 400X)



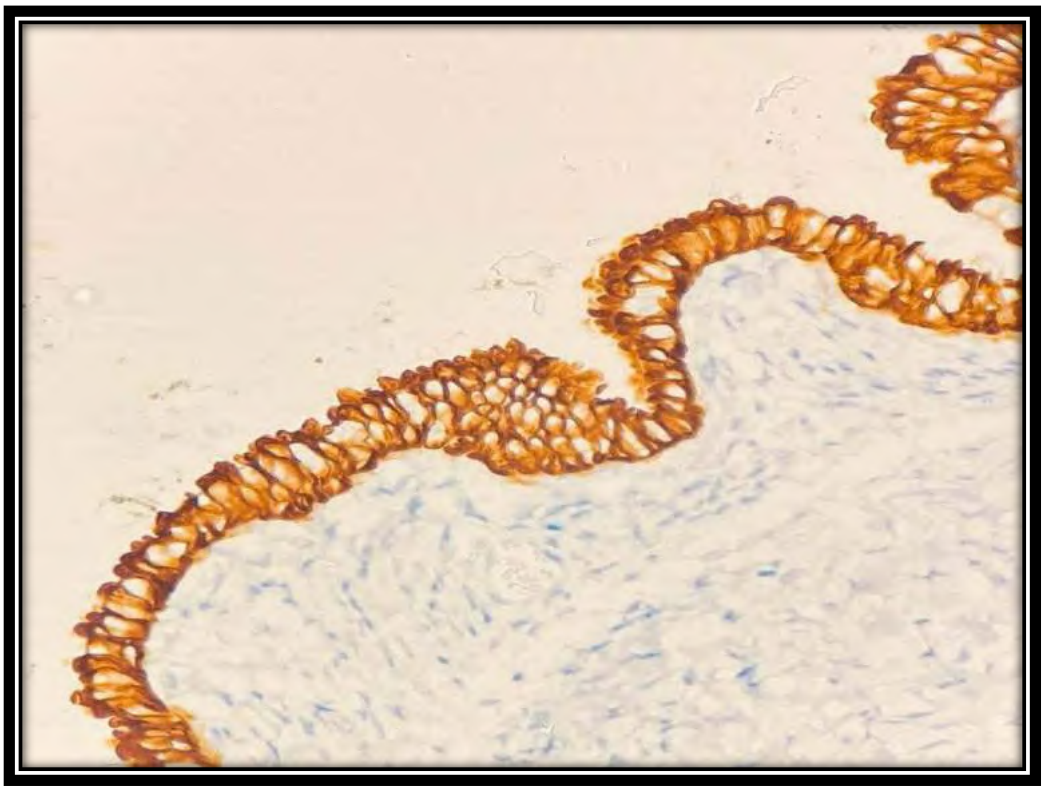
Picture 25- Photomicrograph of seromucinous cystadenoma showing ciliated cells (H&E, 400X)



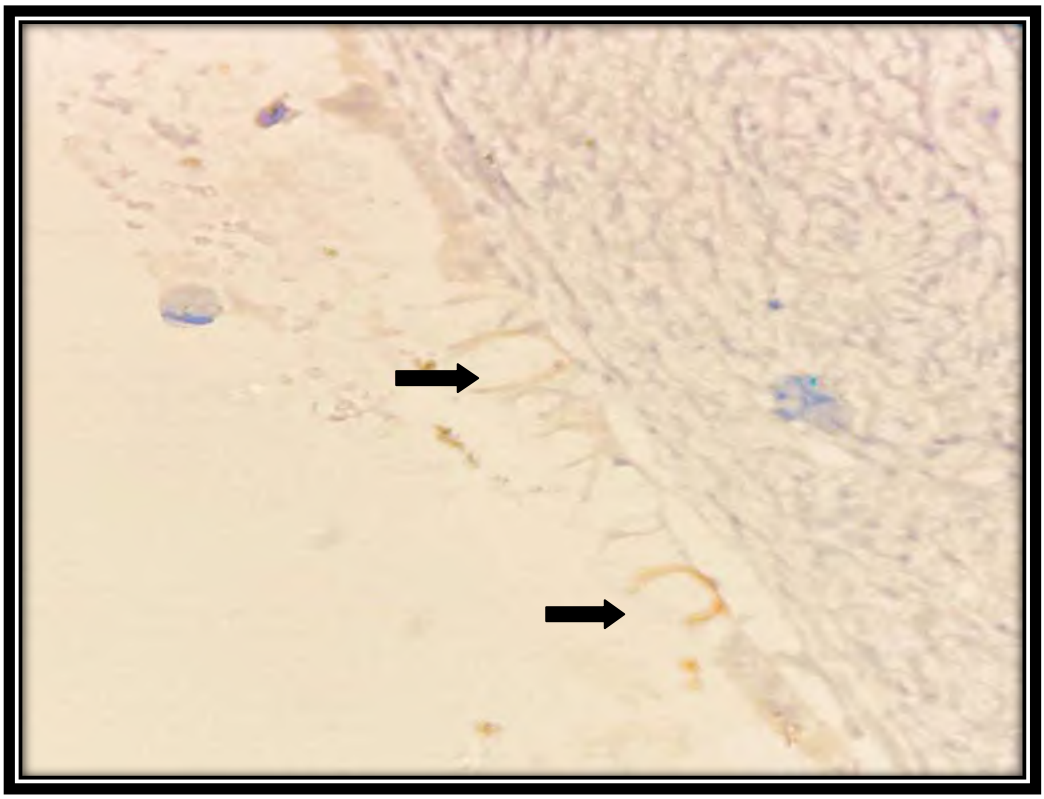
Picture 26- Photomicrograph of seromucinous cystadenoma showing mucin cells (H&E, 400X)



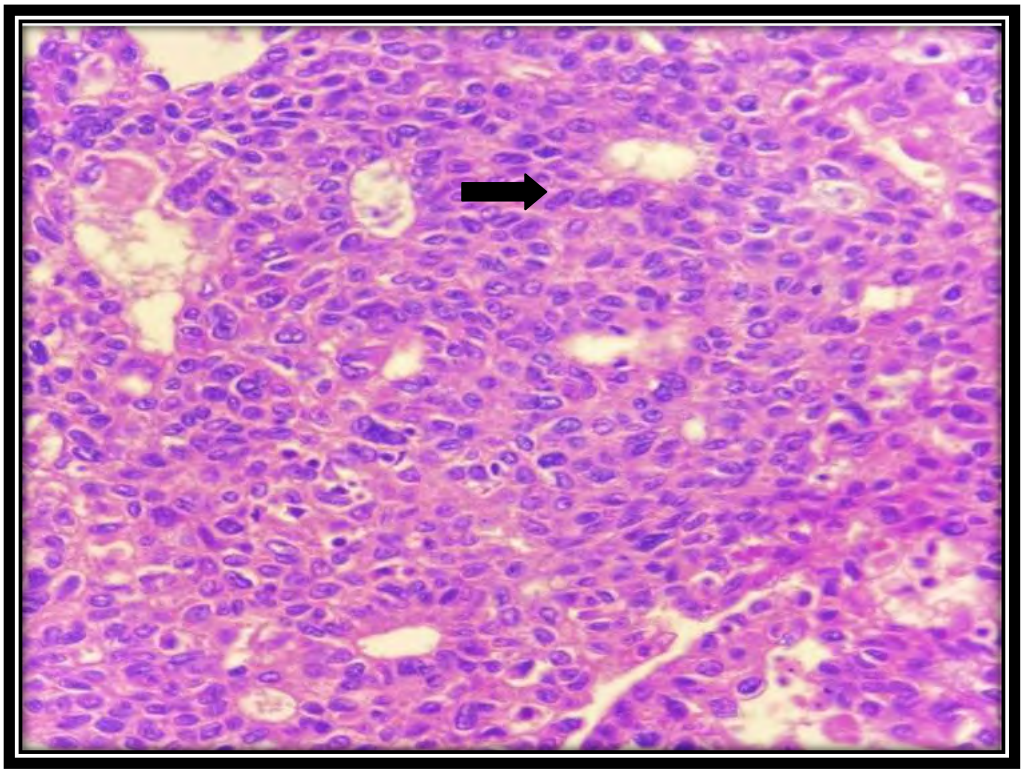
Picture 27- Photomicrograph of seromucinous cystadenoma showing diffuse nuclear WT1 positivity in ciliated cells (IHC, 400X)



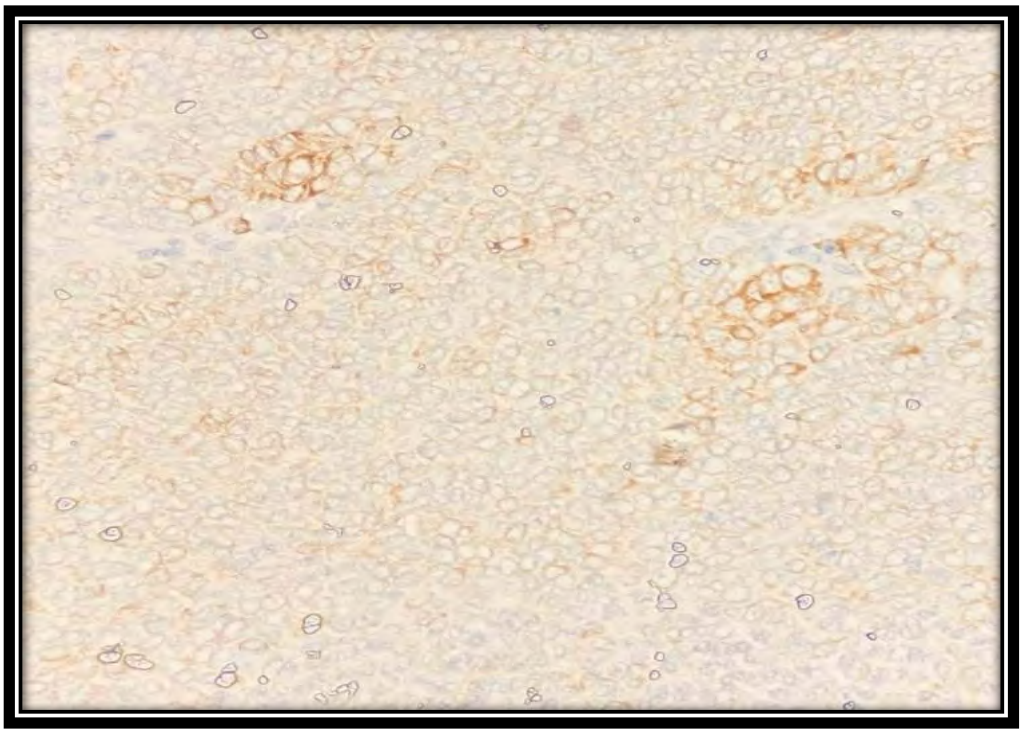
Picture 28- Photomicrograph of seromucinous cystadenoma showing diffuse cytoplasmic CK7 positivity (IHC, 400X)



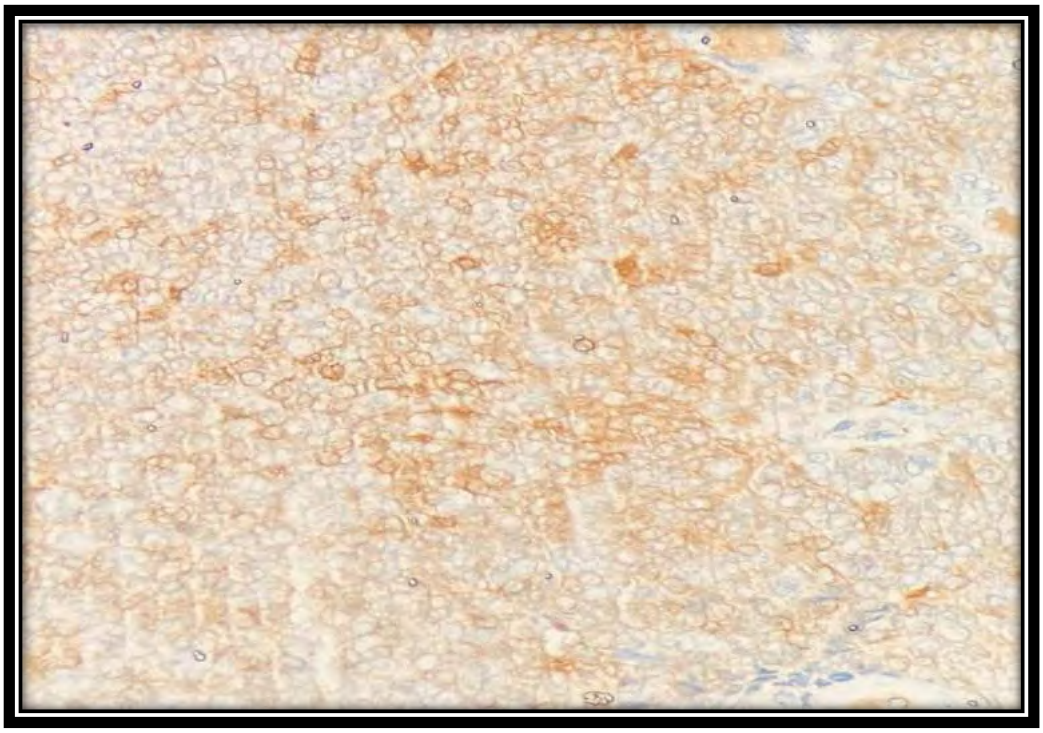
Picture 29- Photomicrograph of seromucinous cystadenoma showing weak cytoplasmic CK20 positivity (IHC, 400X)



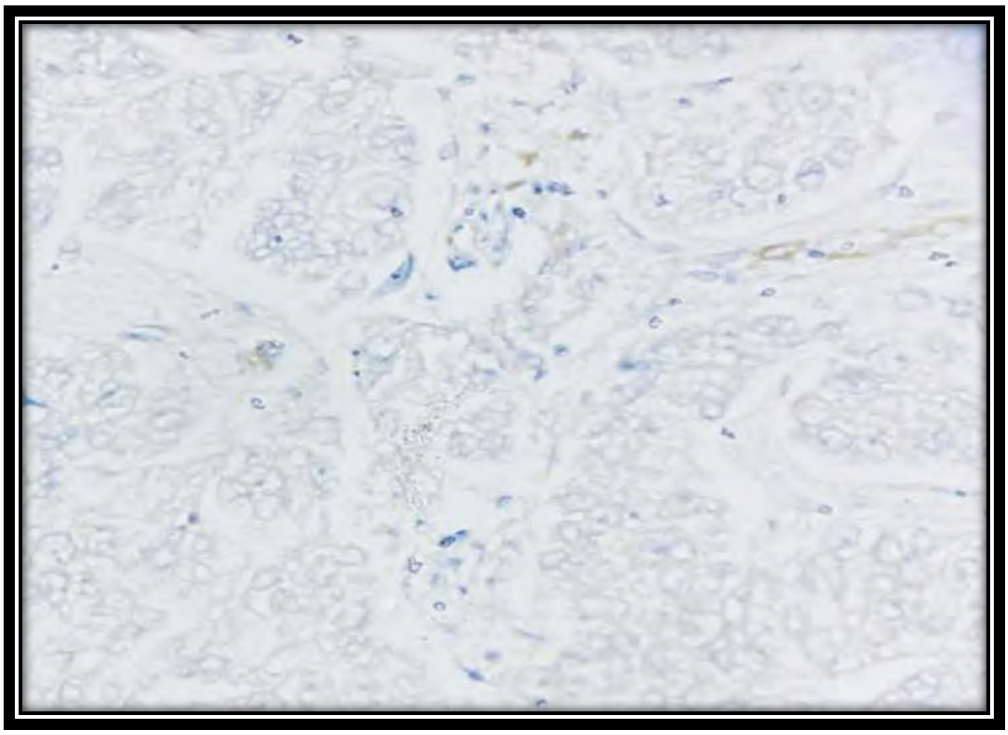
Picture 30- Photomicrograph of adult granulosa cell tumour showing Call Exner bodies and nuclear grooves (Arrow) (H&E,400X)



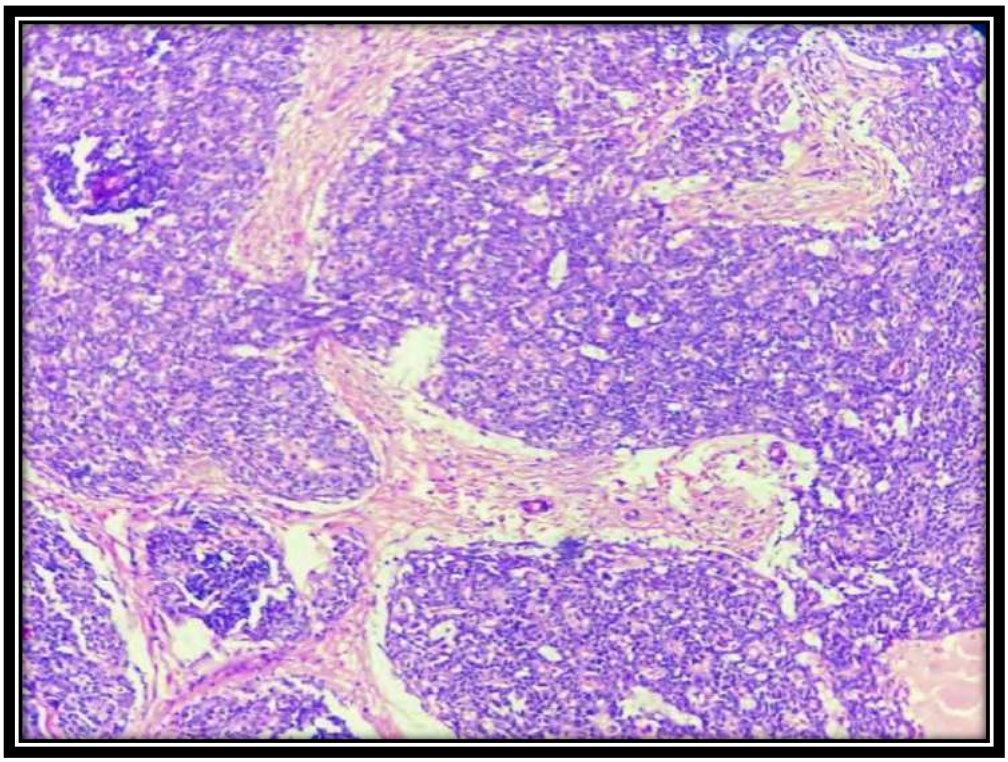
Picture 31- Photomicrograph of adult granulosa cell tumour showing focal cytoplasmic Inhibin positivity (IHC, 400X)



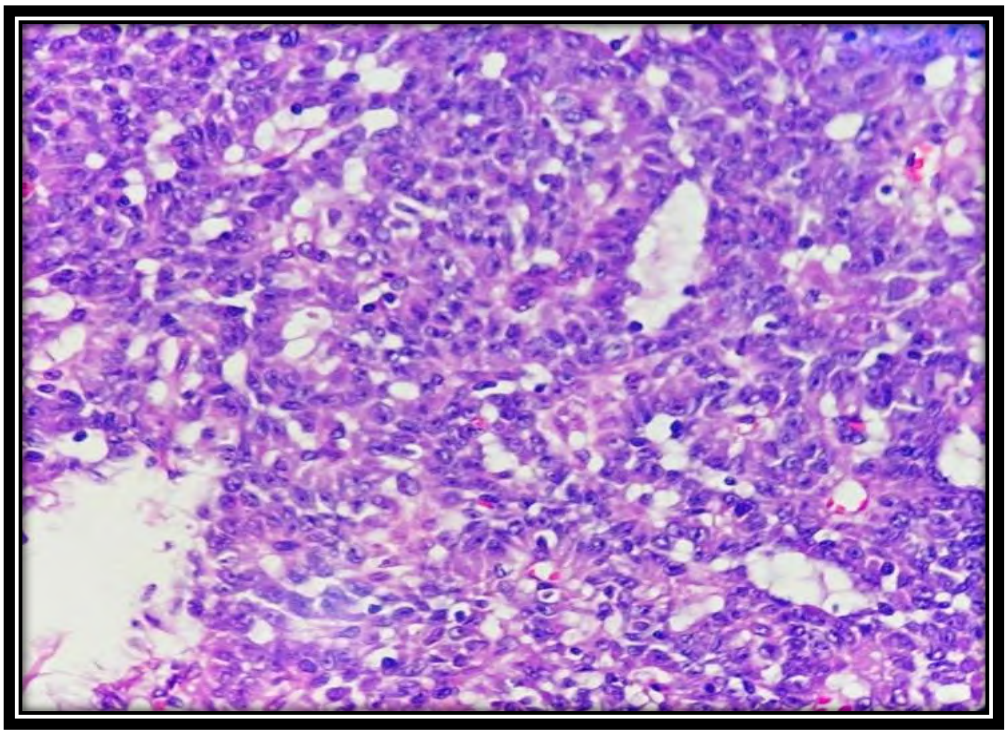
Picture 32 - Photomicrograph of adult granulosa cell tumour showing diffuse cytoplasmic Calretinin positivity (IHC, 400X)



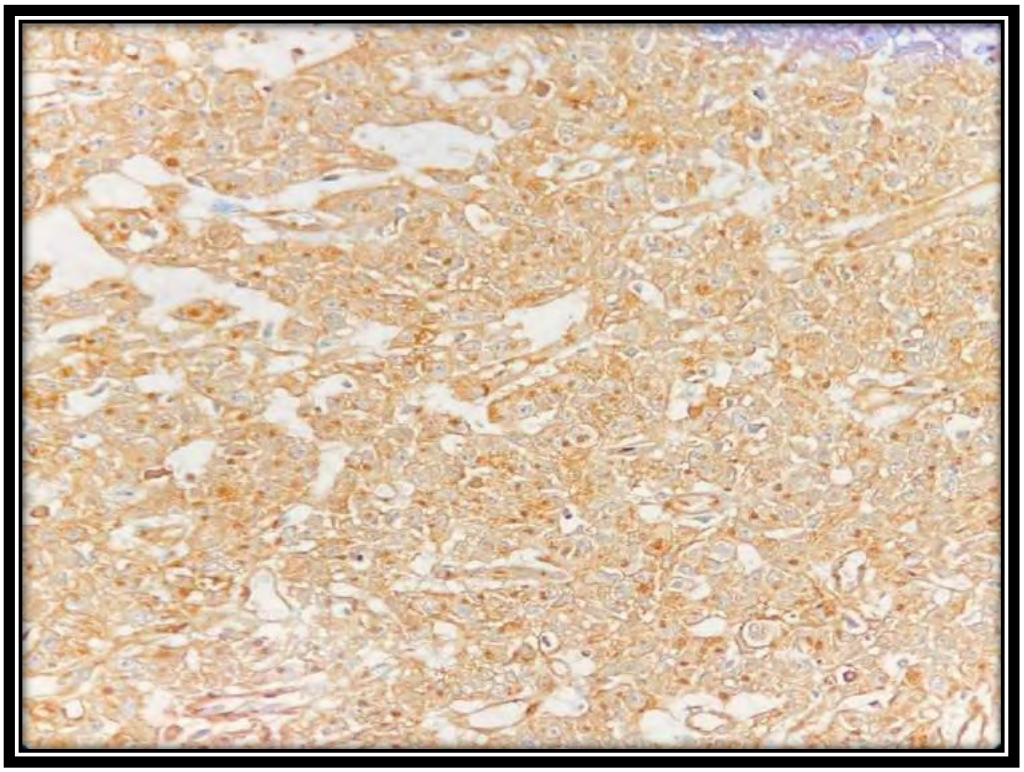
Picture 33- Photomicrograph of adult granulosa cell tumour showing WT1 negativity (IHC, 400X



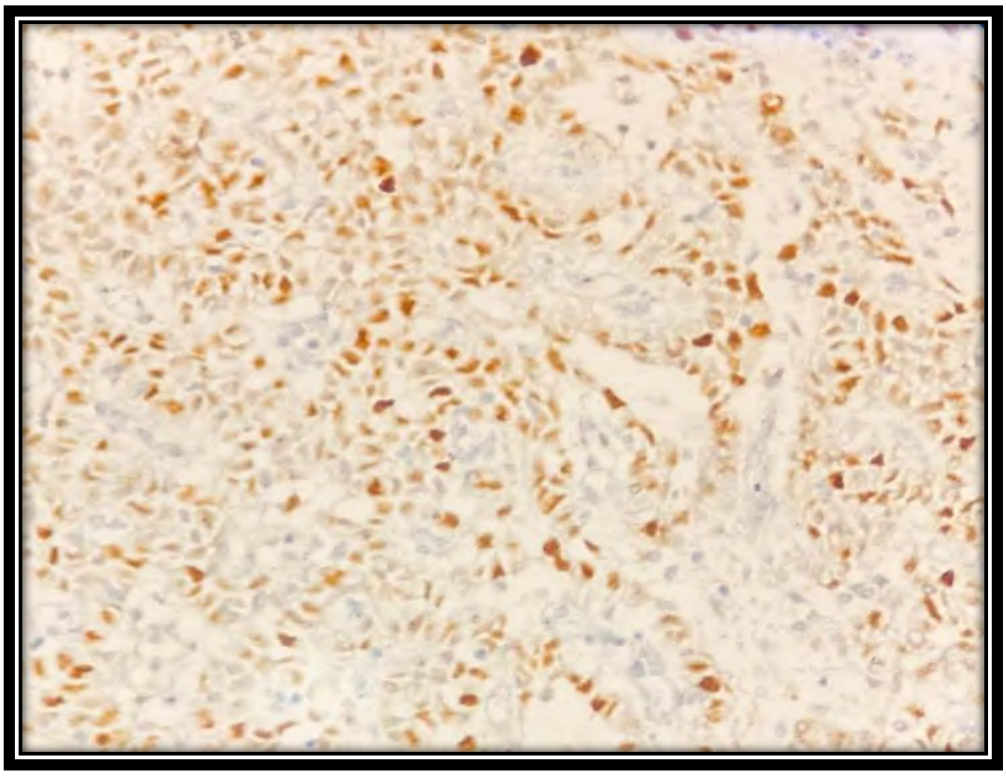
Picture 34- Photomicrograph of juvenile granulosa cell tumour showing tumour arranged in follicles of varied morphology. (H&E, 100X)



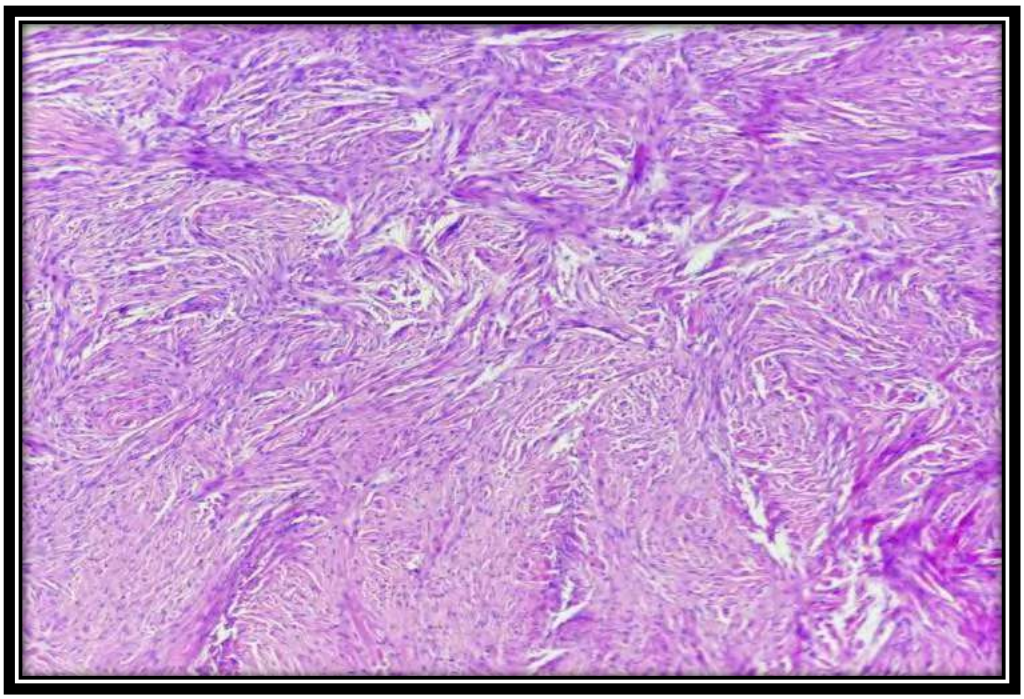
Picture 35- Photomicrograph of juvenile granulosa cell tumour showing tumour cells without nuclear grooves and pale amphophilic cytoplasm. (H&E, 400X)



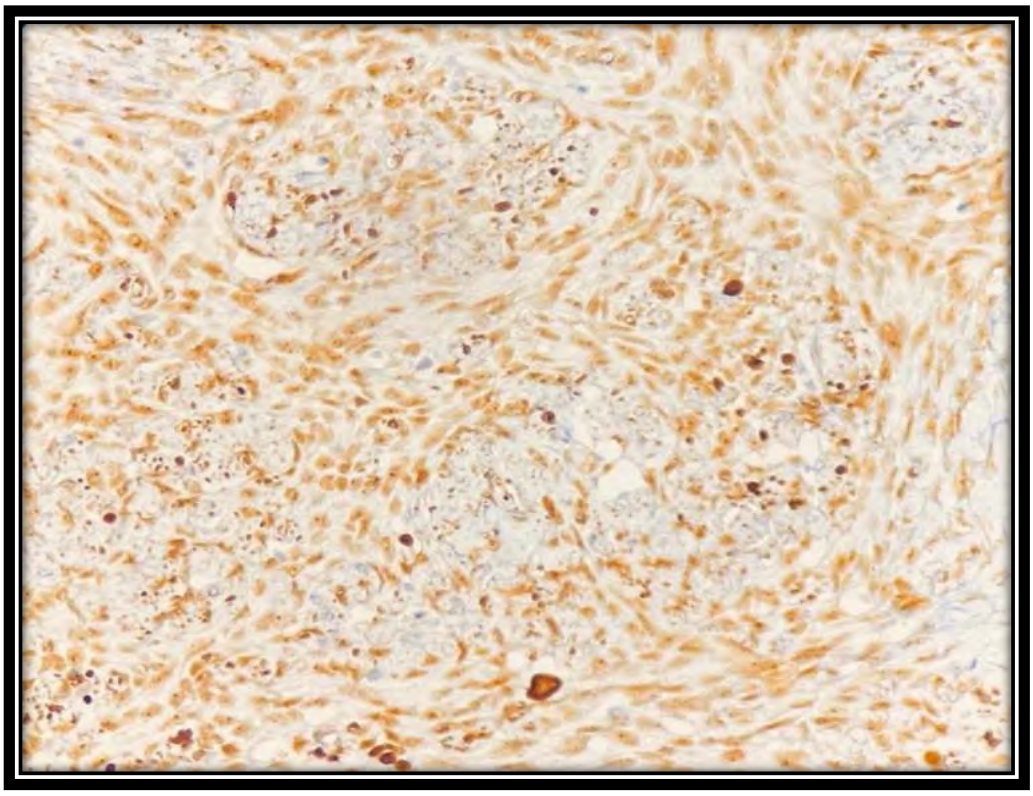
Picture 36- Photomicrograph of juvenile granulosa cell tumour showing diffuse cytoplasmic Calretinin positivity (IHC, 400X)



Picture 37- Photomicrograph of juvenile granulosa cell tumour showing nuclear ER positivity (IHC, 400X)

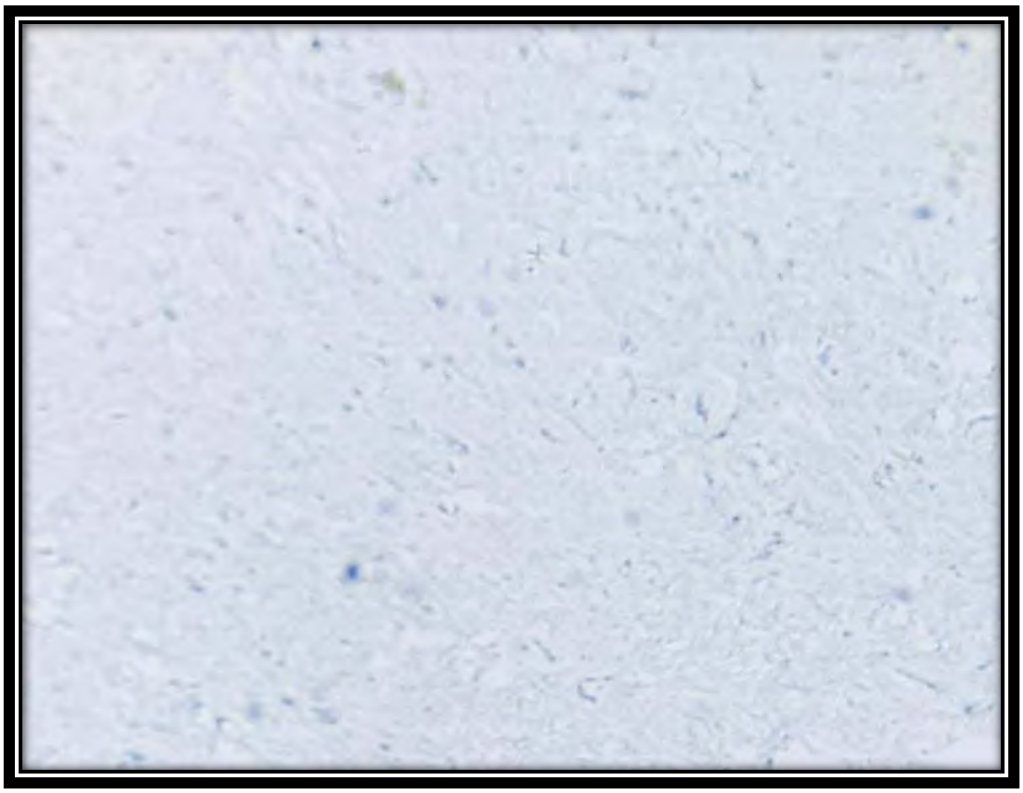


Picture 38 - Photomicrograph of fibroma showing spindle tumour cells present within a collagenized stroma arranged in fascicles (H&E,400X)

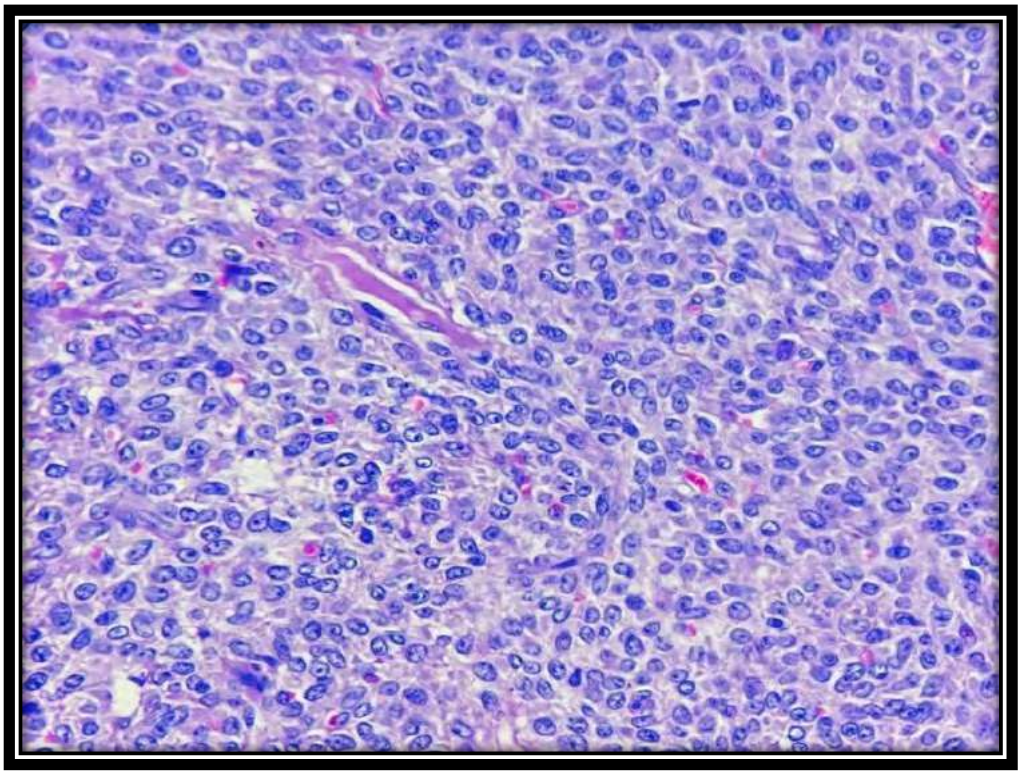


Picture 39 - Photomicrograph of fibroma nuclear positivity of WT1 (IHC,400X)

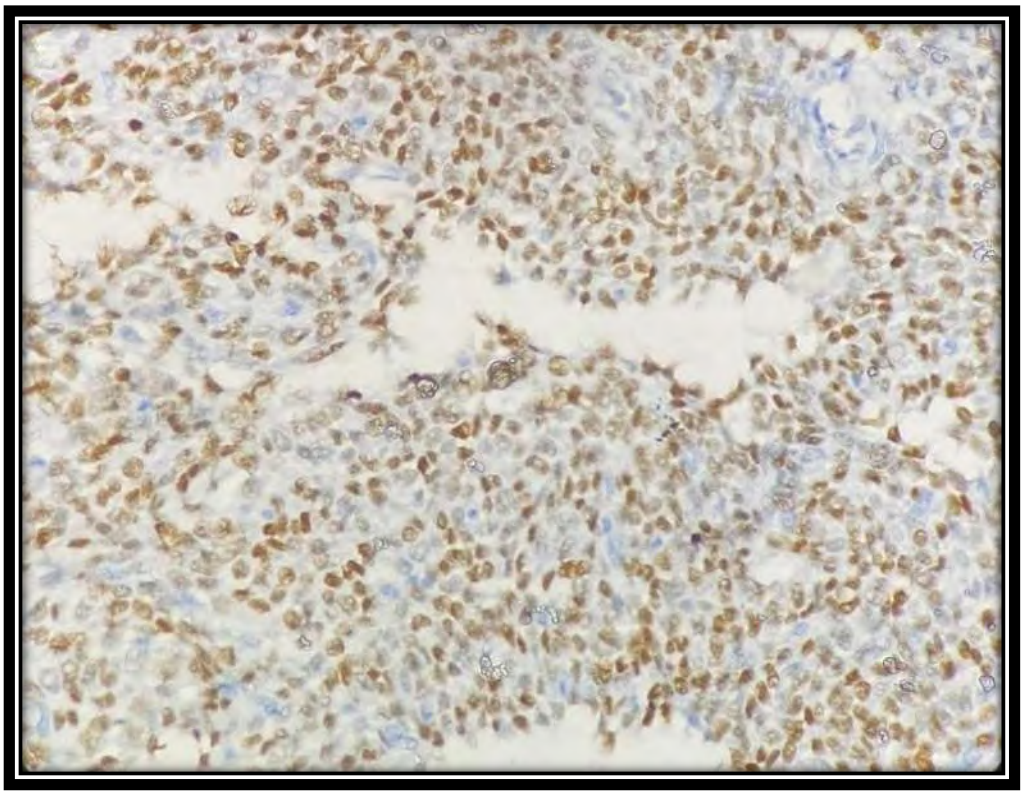
Picture 40 - Photomicrograph of fibroma showing cytoplasmic SMA positivity (IHC,400X)



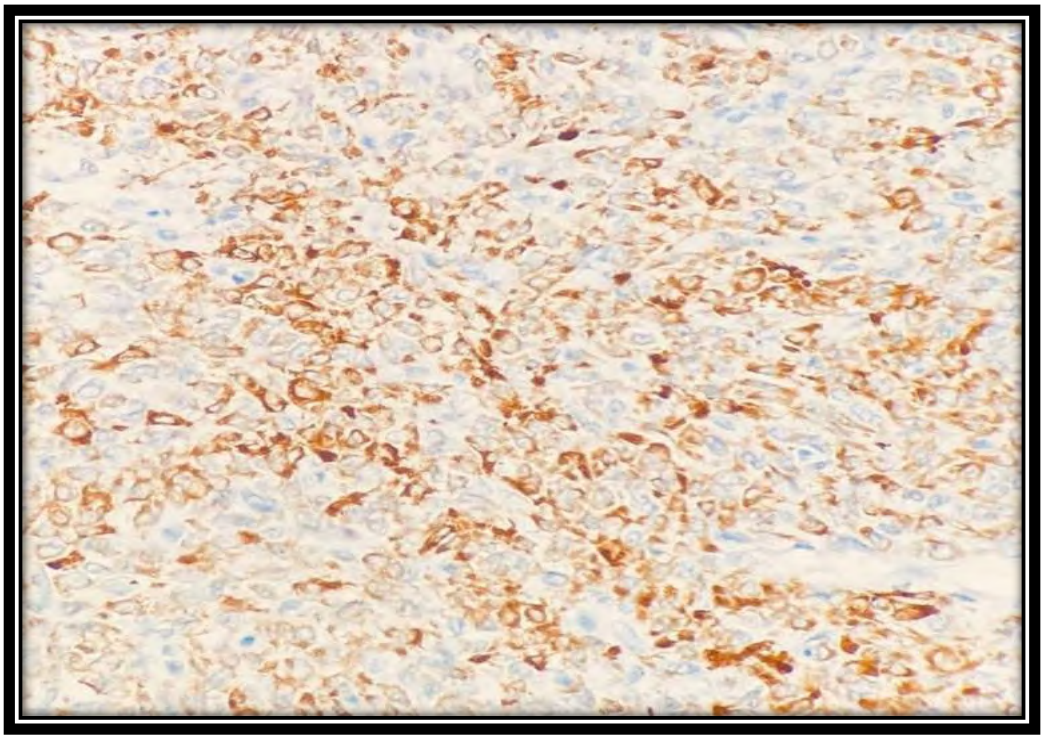
Picture 41 - Photomicrograph of fibroma showing Desmin negativity (IHC,400X)



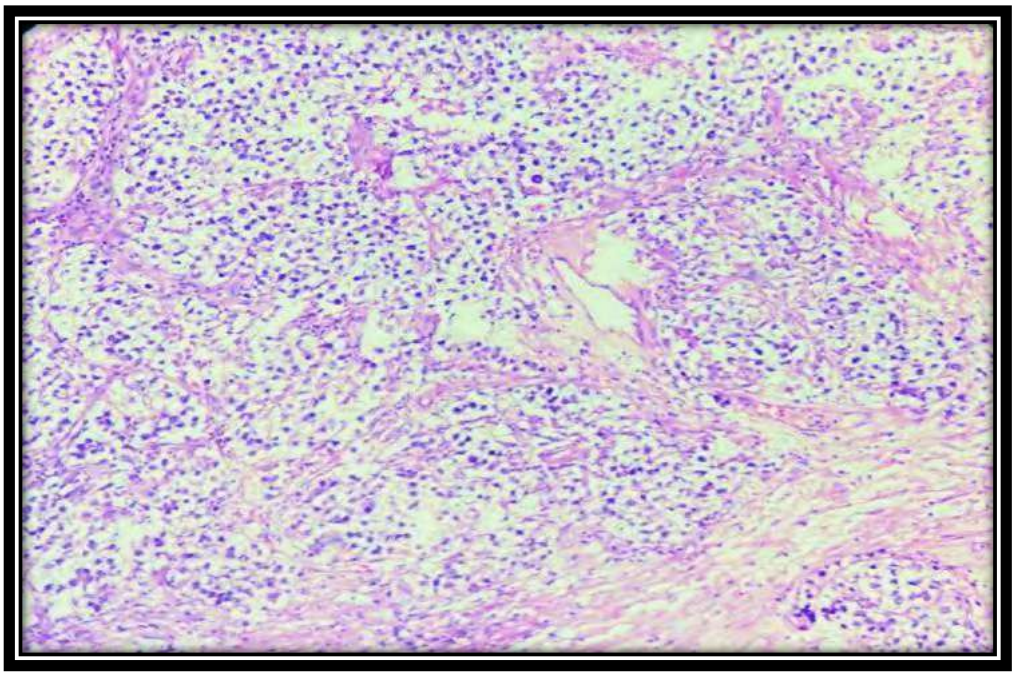
Picture 42 - Photomicrograph of thecoma showing round to oval nuclei and few delicate blood vessels (H&E,400X)



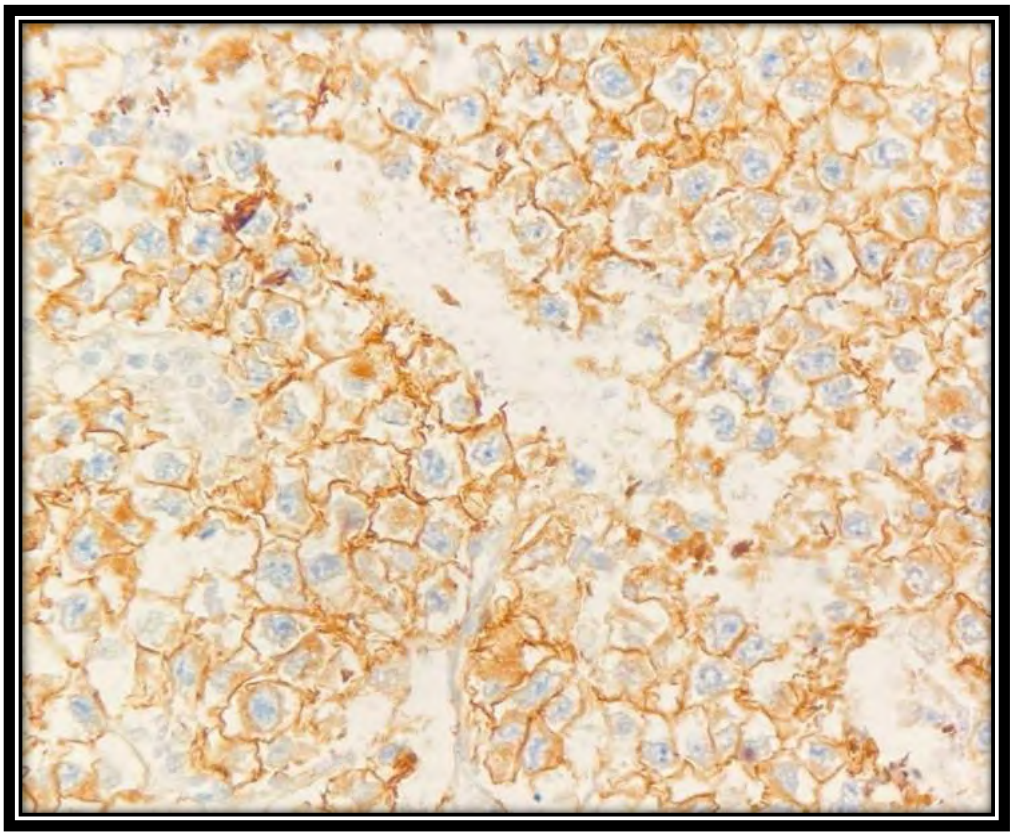
Picture 43 - Photomicrograph of thecoma showing nuclear positivity of ER (IHC,400X)



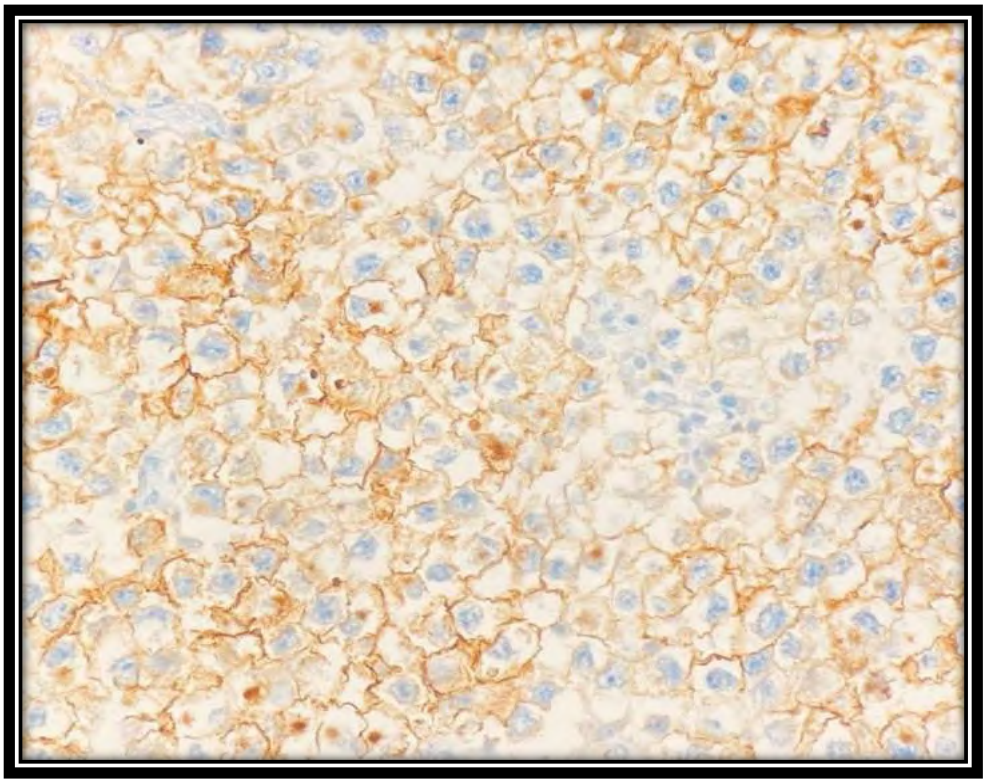
Picture 44 - Photomicrograph of thecoma showing diffuse cytoplasmic Inhibin positivity (IHC,400X)



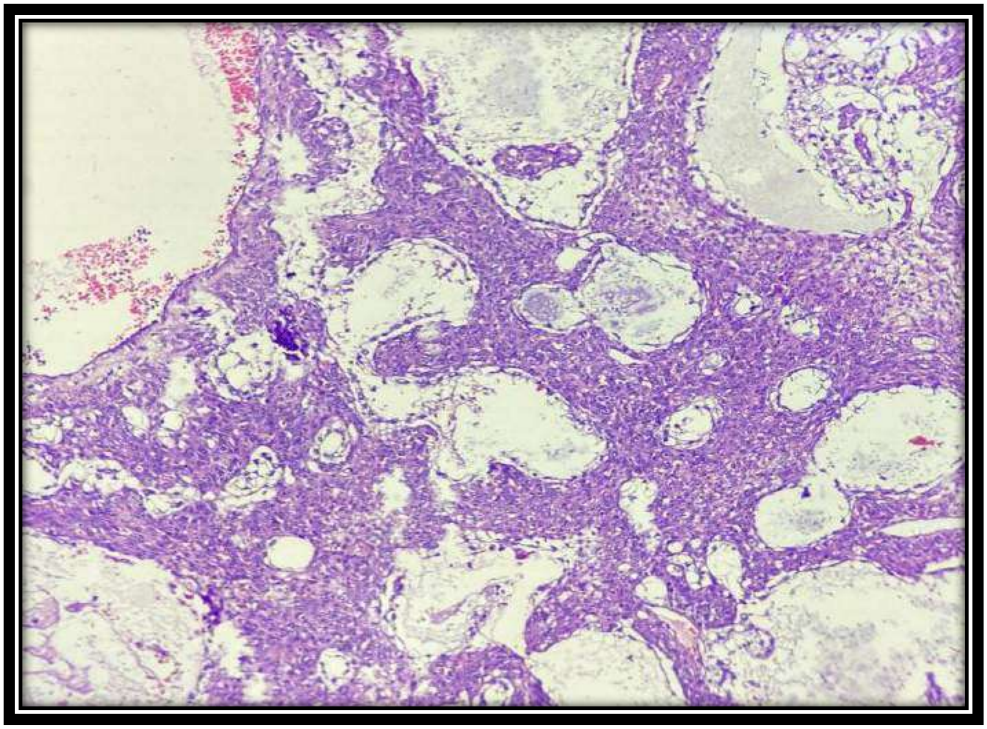
Picture 45- Photomicrograph of dysgerminoma showing tumour arranged in nests separated by fibrous septa, infiltrated by lymphocytes (H&E, 100X)



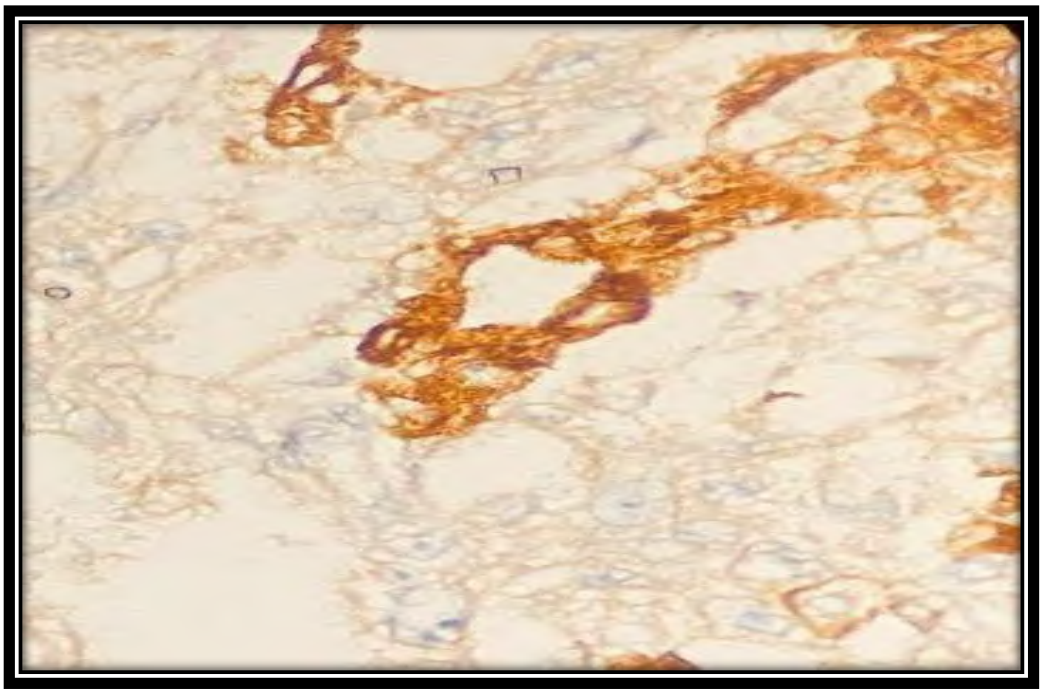
Picture 46- Photomicrograph of dysgerminoma showing diffuse cytoplasmic CD117 positivity (IHC, 400X)



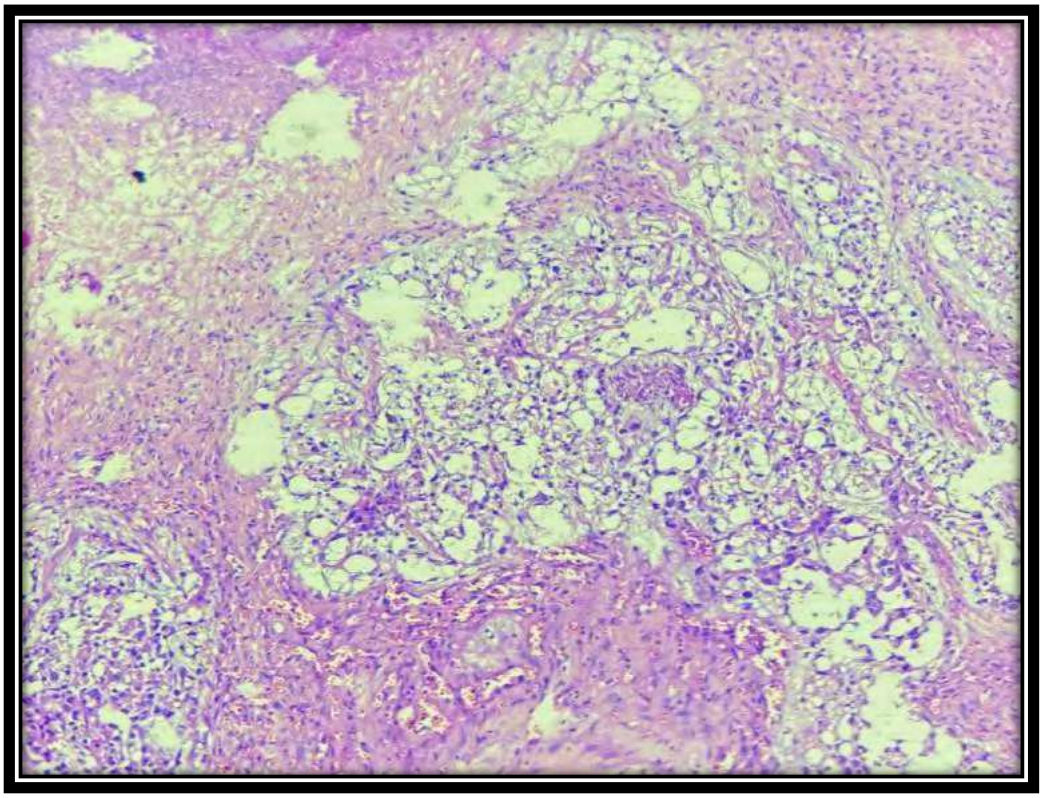
Picture 47- Photomicrograph of dysgerminoma showing diffuse cytoplasmic PLAP positivity (IHC, 400X)



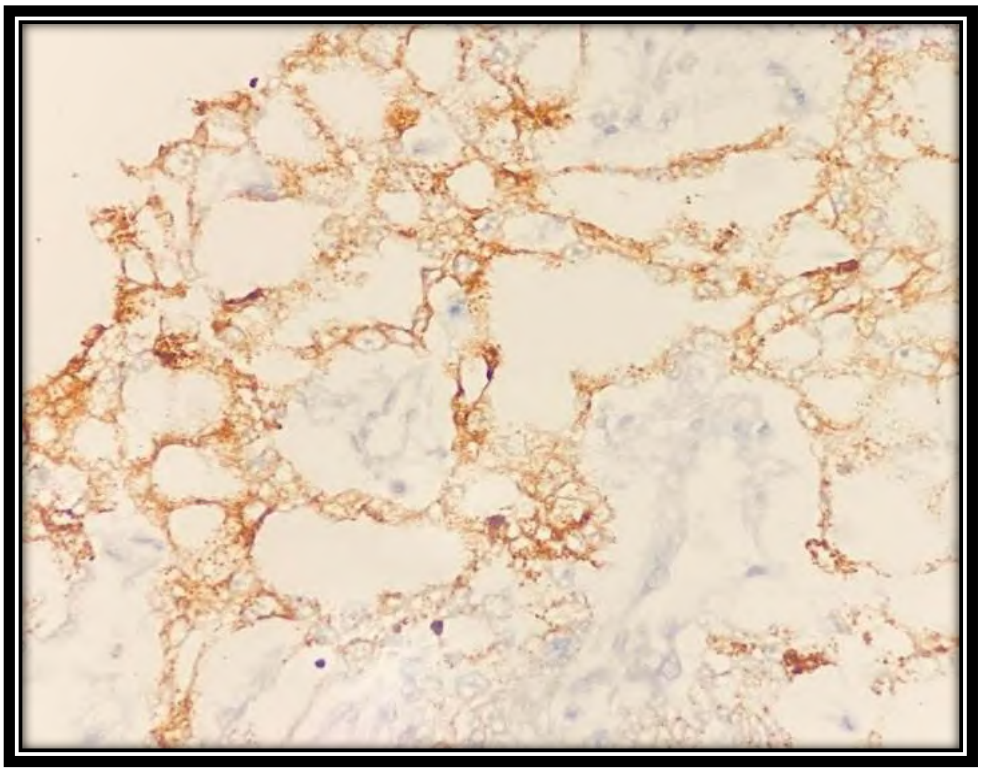
Picture 48- Photomicrograph of yolk sac tumour arranged in cystic pattern (H&E,100X)



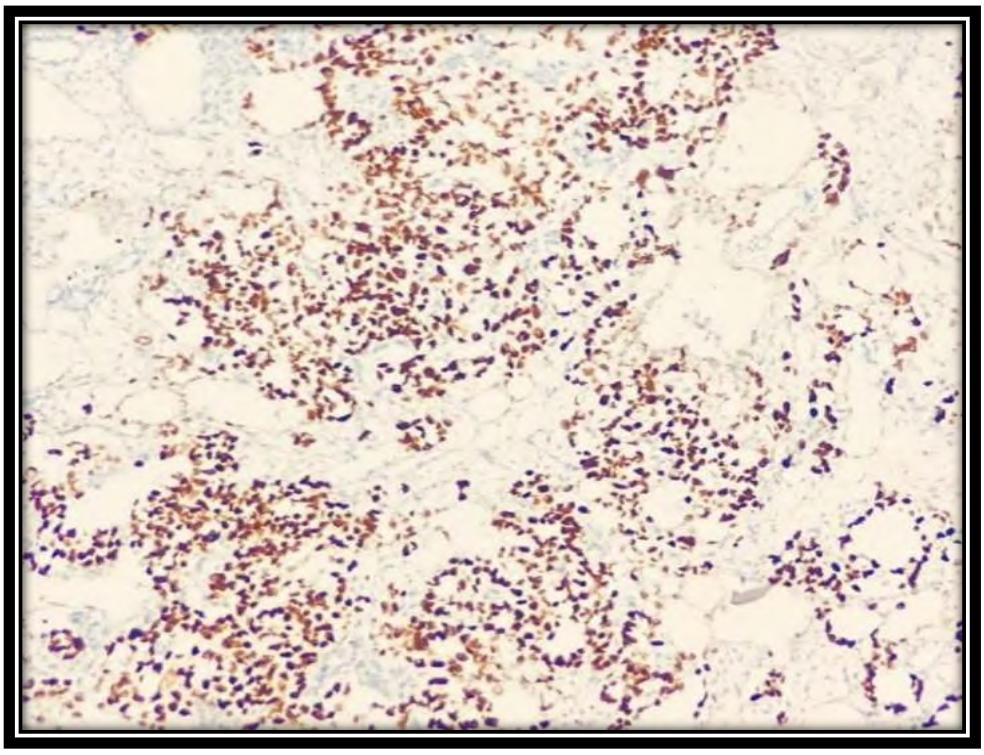
Picture 49- Photomicrograph of yolk sac tumour showing cytoplasmic AFP positivity (IHC,400X)



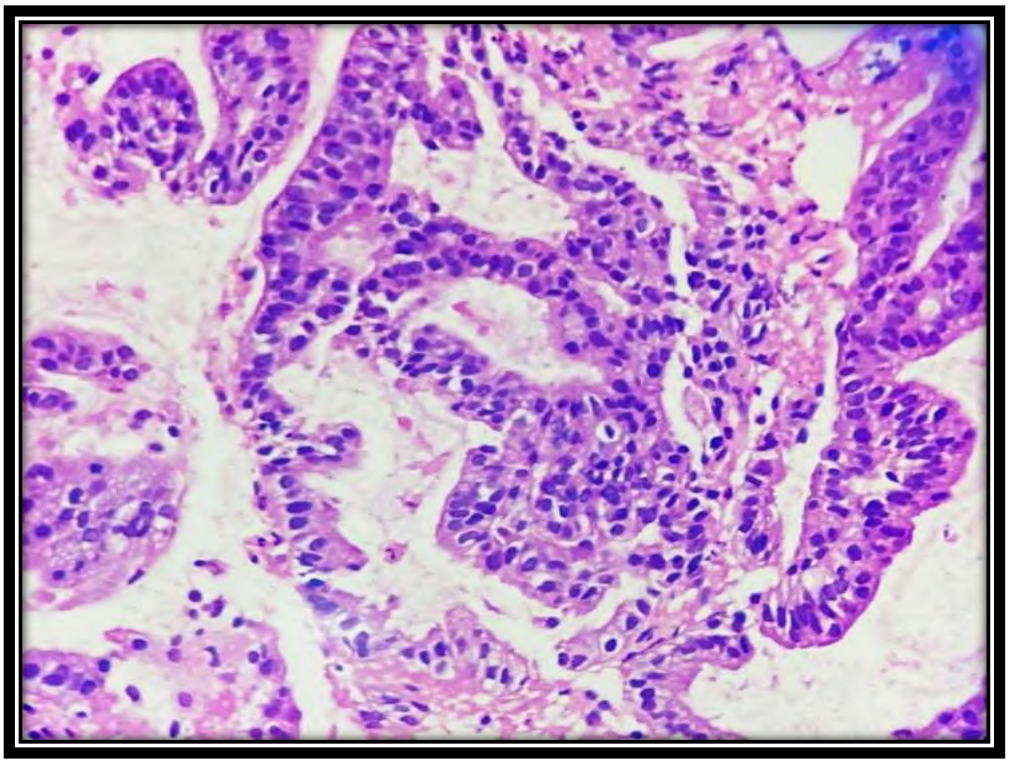
Picture 50- Photomicrograph of yolk sac tumour showing reticular pattern (H&E,100X)



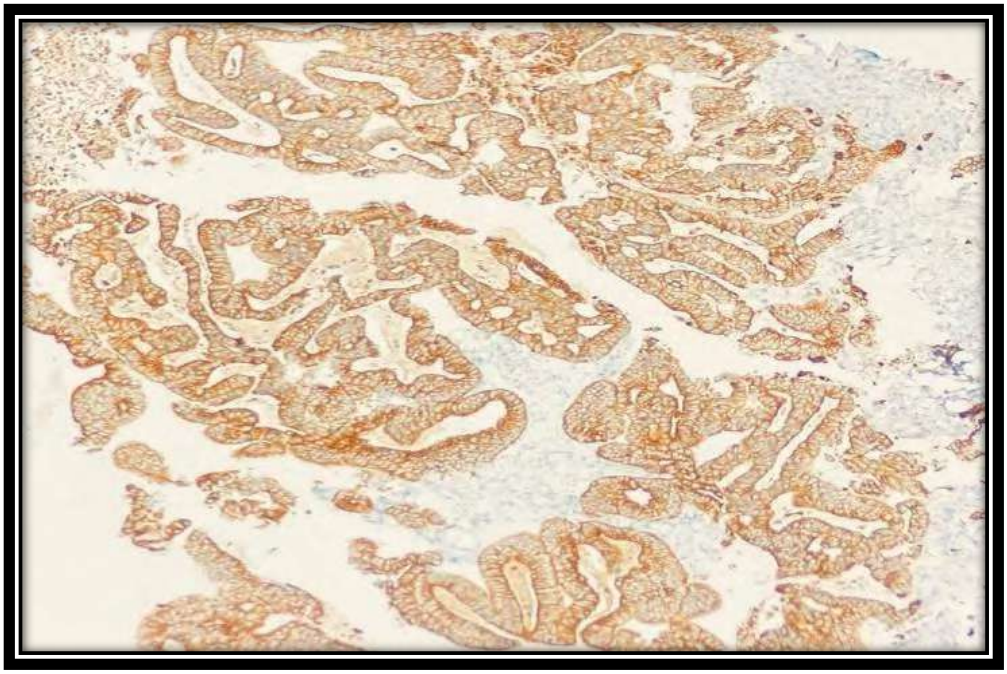
Picture 51 - Photomicrograph of yolk sac tumour showing diffuse cytoplasmic Glypican 3 positivity. (IHC, 100X)



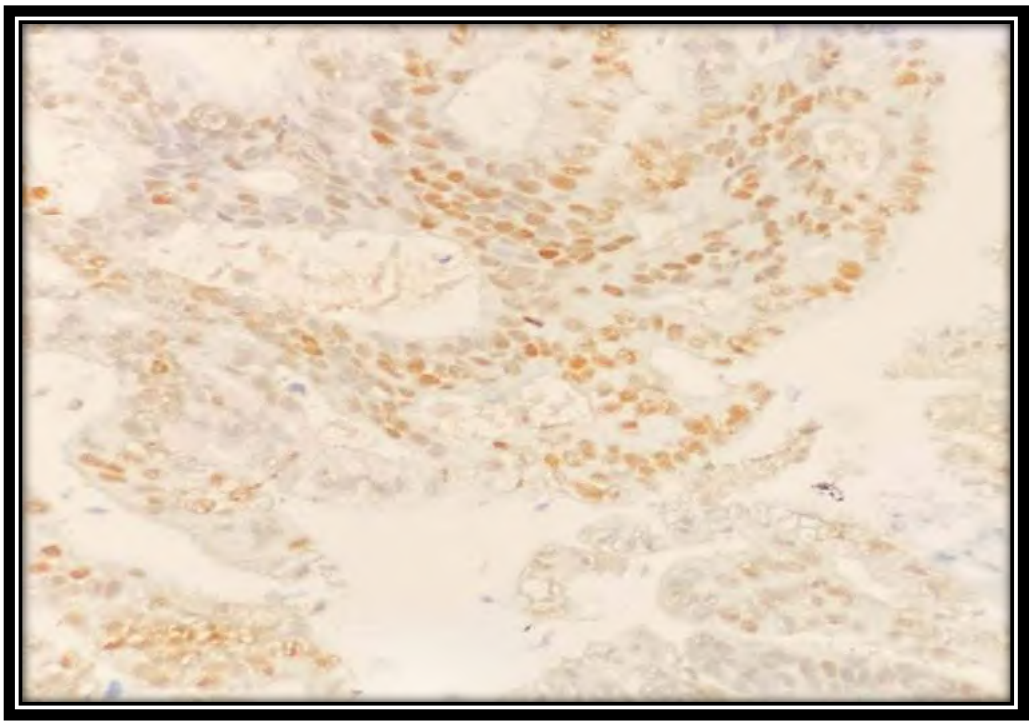
Picture 52- Photomicrograph of yolk sac tumour showing diffuse nuclear SALL4 positivity. (IHC, 100X)



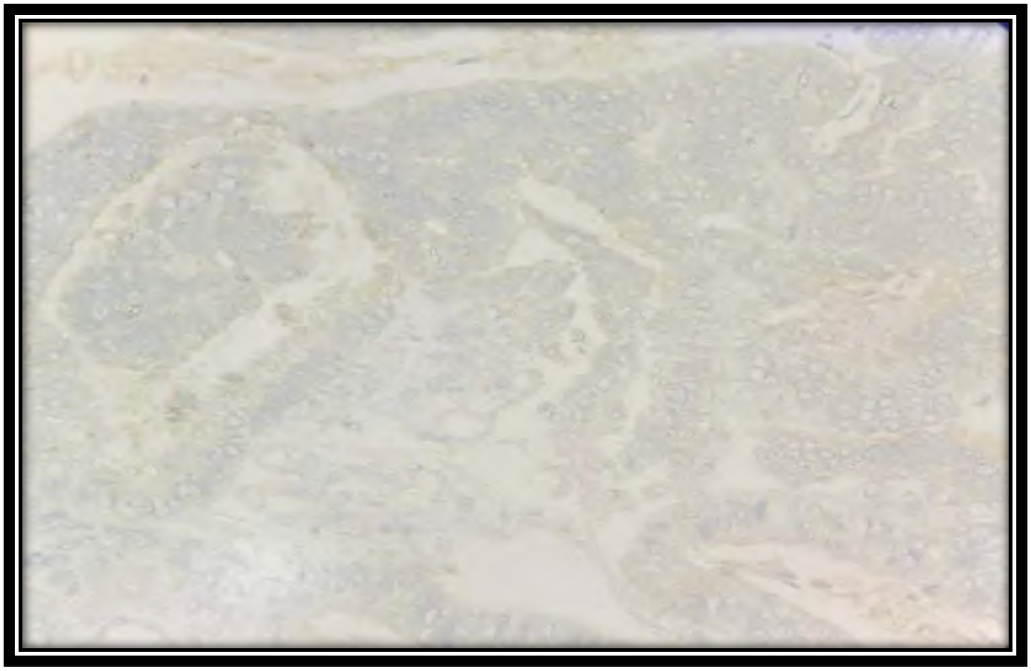
Picture 53- Photomicrograph showing metastatic adenocarcinomatous deposits from duodenum to ovary arranged in glandular configuration (H&E, 400X)



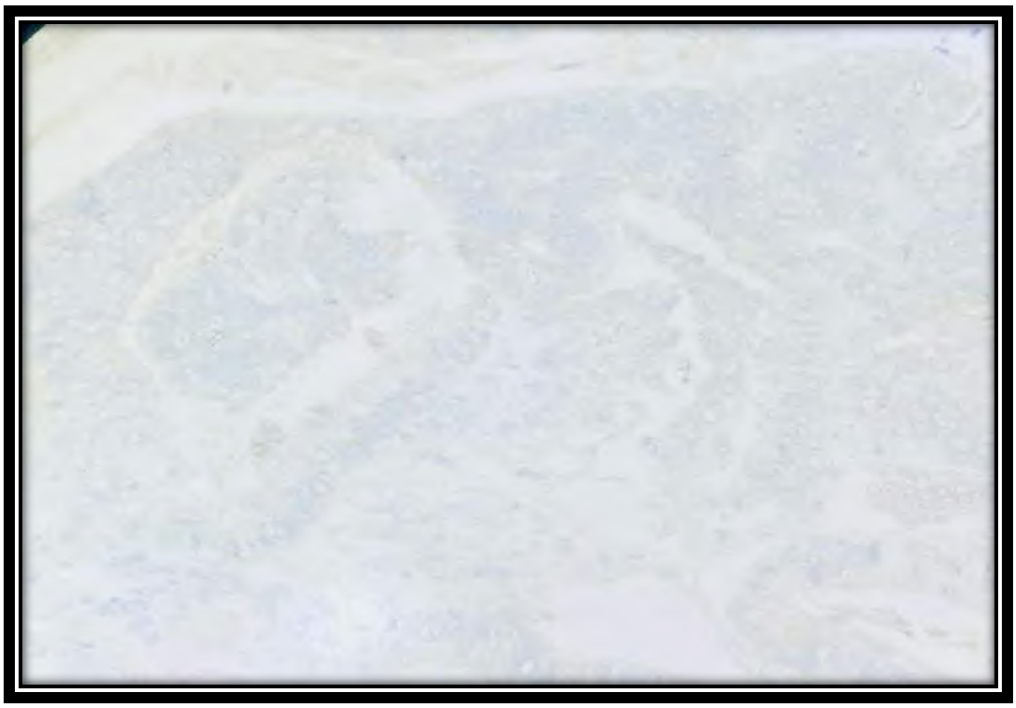
Picture 54- Photomicrograph of metastatic adenocarcinomatous deposits from duodenum to ovary showing diffuse cytoplasmic CK7 positivity (IHC, 400X)



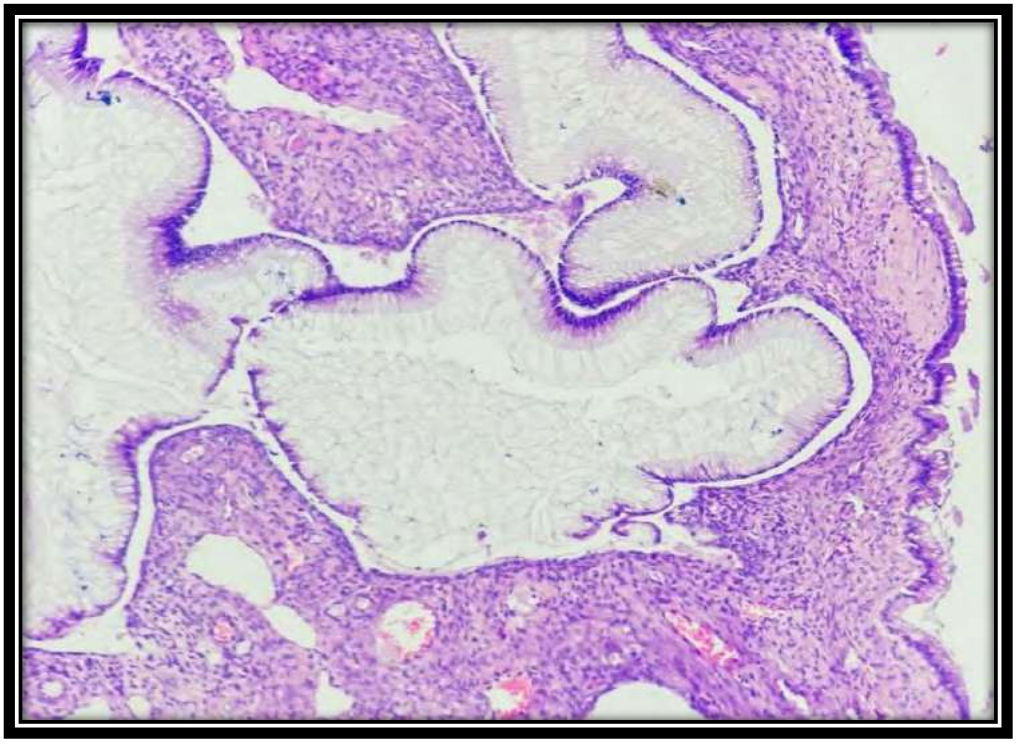
Picture 55- Photomicrograph of metastatic adenocarcinomatous deposits from duodenum to ovary showing nuclear CDX2 positivity (IHC, 400X)



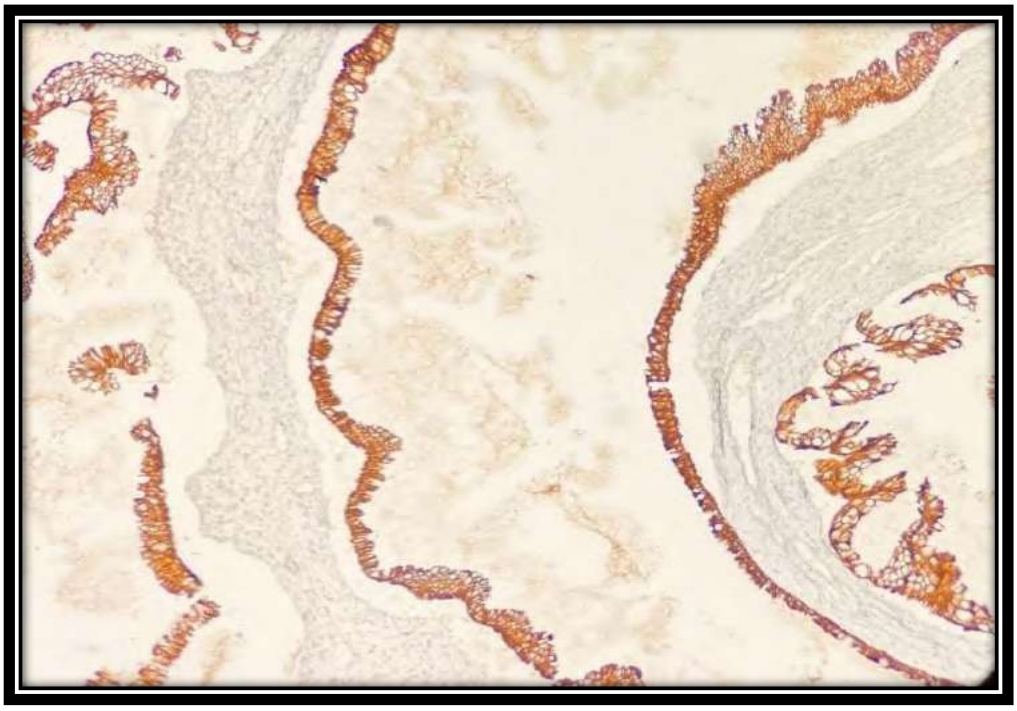
Picture 56- Photomicrograph of metastatic adenocarcinomatous deposits from duodenum to ovary showing CK20 negativity (IHC, 400X)



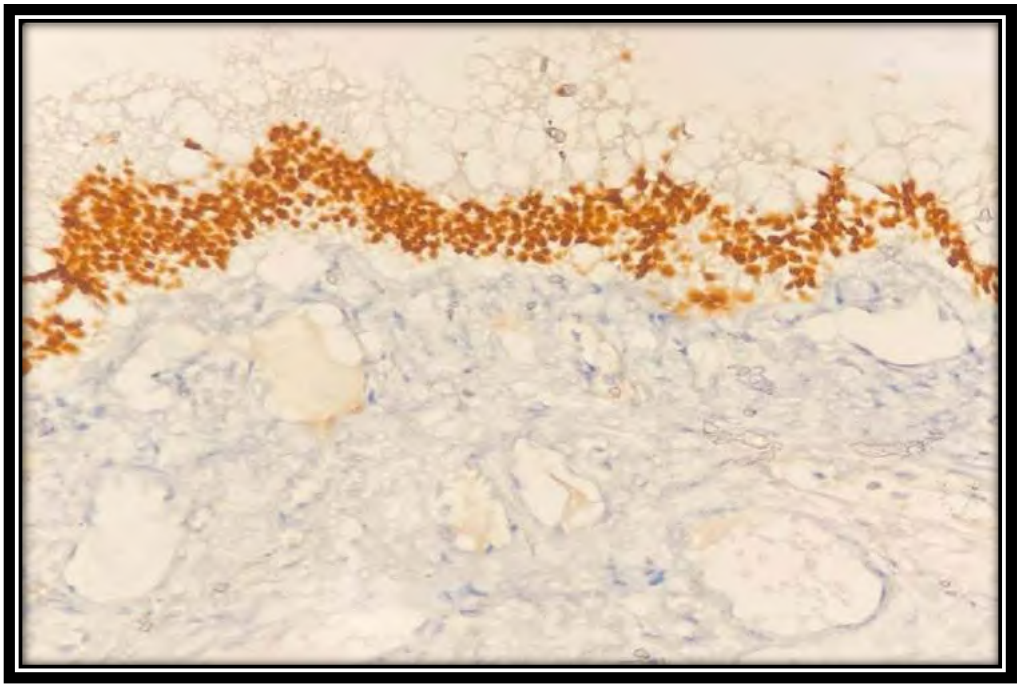
Picture 57- Photomicrograph of metastatic adenocarcinomatous deposits from duodenum to ovary showing PAX8 negativity (IHC, 400X)



Picture 58- Photomicrograph of metastatic ductal adenocarcinomatous deposits of pancreas to ovary showing tumour arranged in glandular configuration having abundant cytoplasm (H&E, 400X)

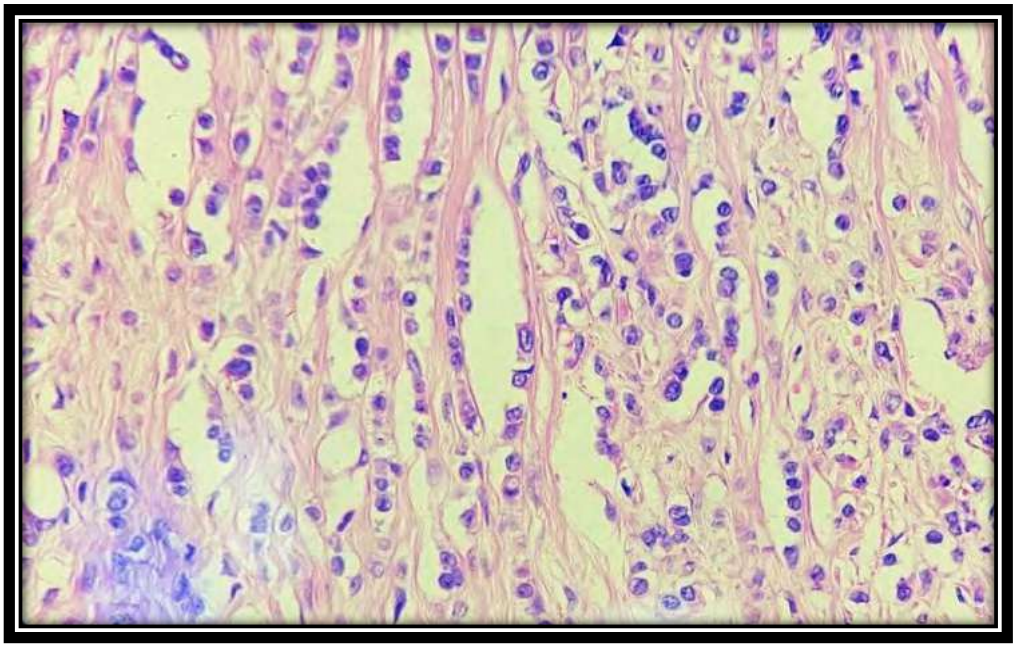


Picture 59- Photomicrograph of metastatic ductal adenocarcinomatous deposits of pancreas to ovary showing diffuse cytoplasmic CK7 positivity (IHC, 100X)

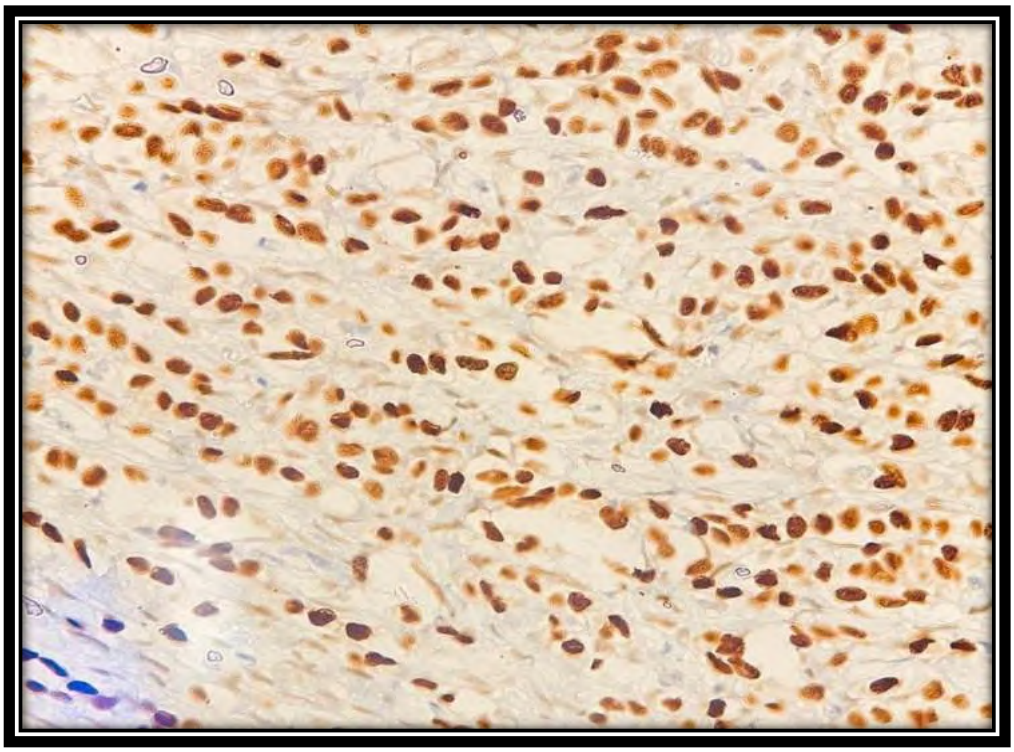


Picture 60- Photomicrograph of metastatic ductal adenocarcinomatous deposits of pancreas to ovary showing diffuse nuclear CDX2 positivity (IHC, 400X)

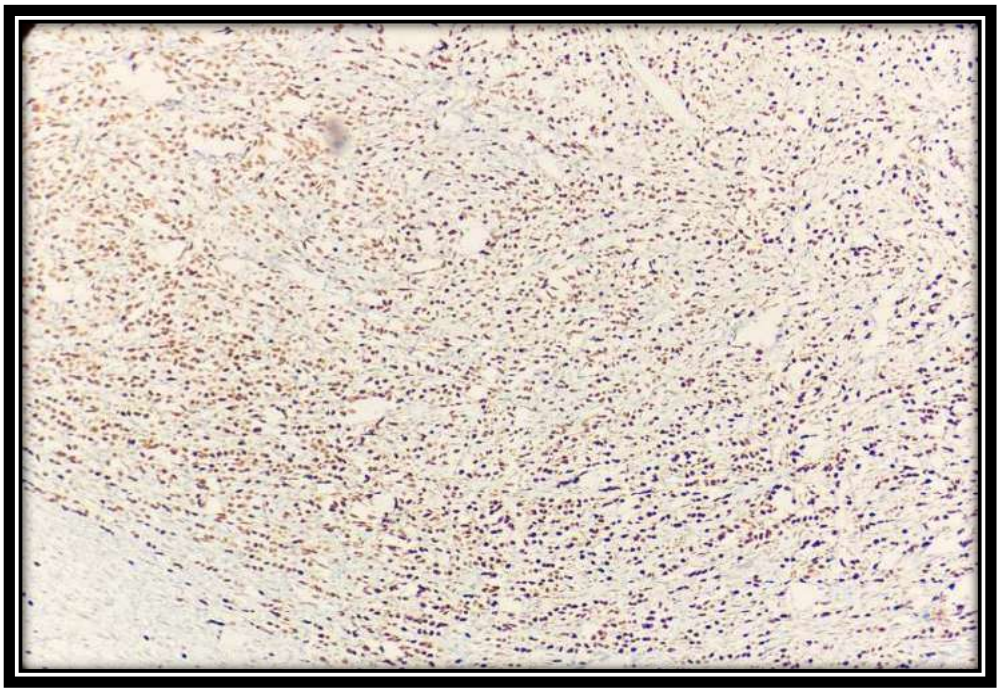
Picture 61- Photomicrograph of metastatic ductal adenocarcinomatous deposits of pancreas to ovary showing CK20 negativity (IHC, 100X)



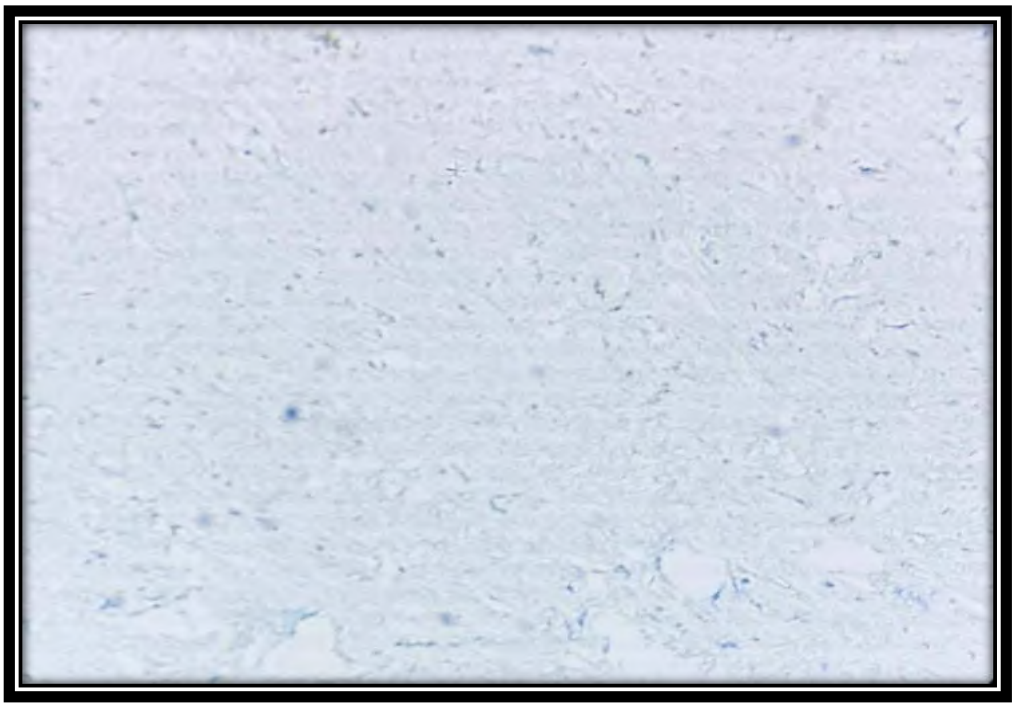
Picture 62- Photomicrograph of showing metastatic lobular breast carcinoma to ovaries depicting Indian file pattern (H&E, 400X)



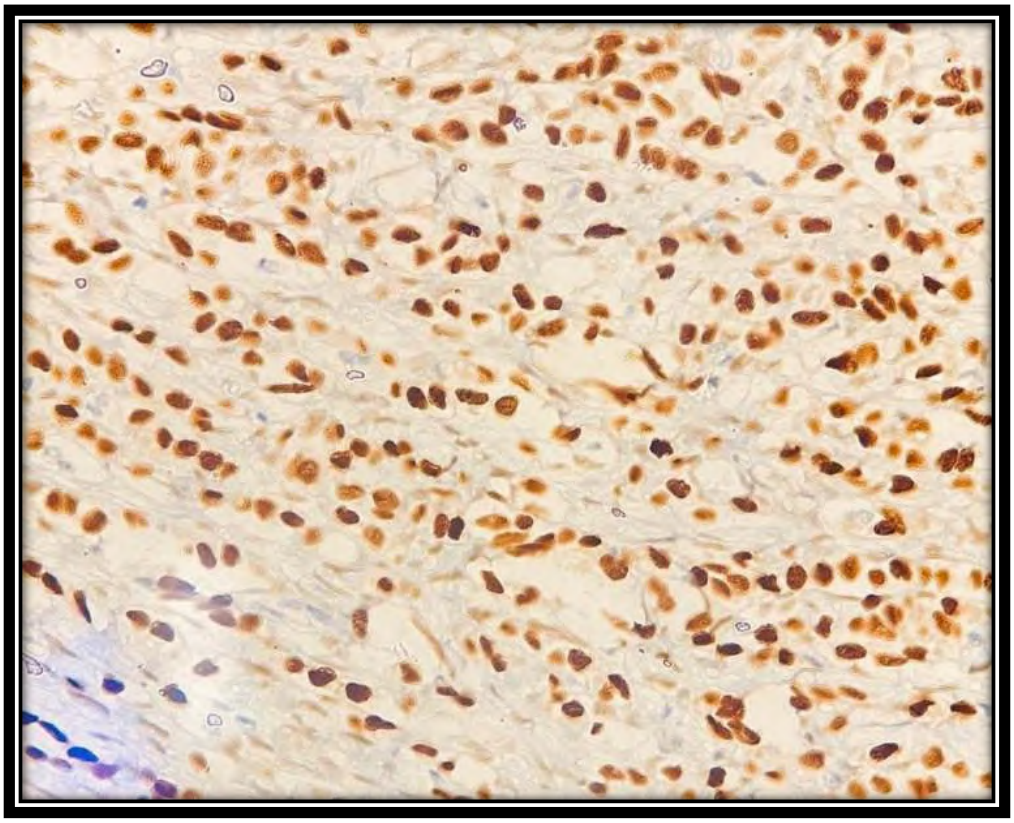
Picture 63- Photomicrograph of showing metastatic lobular breast carcinoma to ovaries showing diffuse nuclear ER positivity (H&E, 400X)



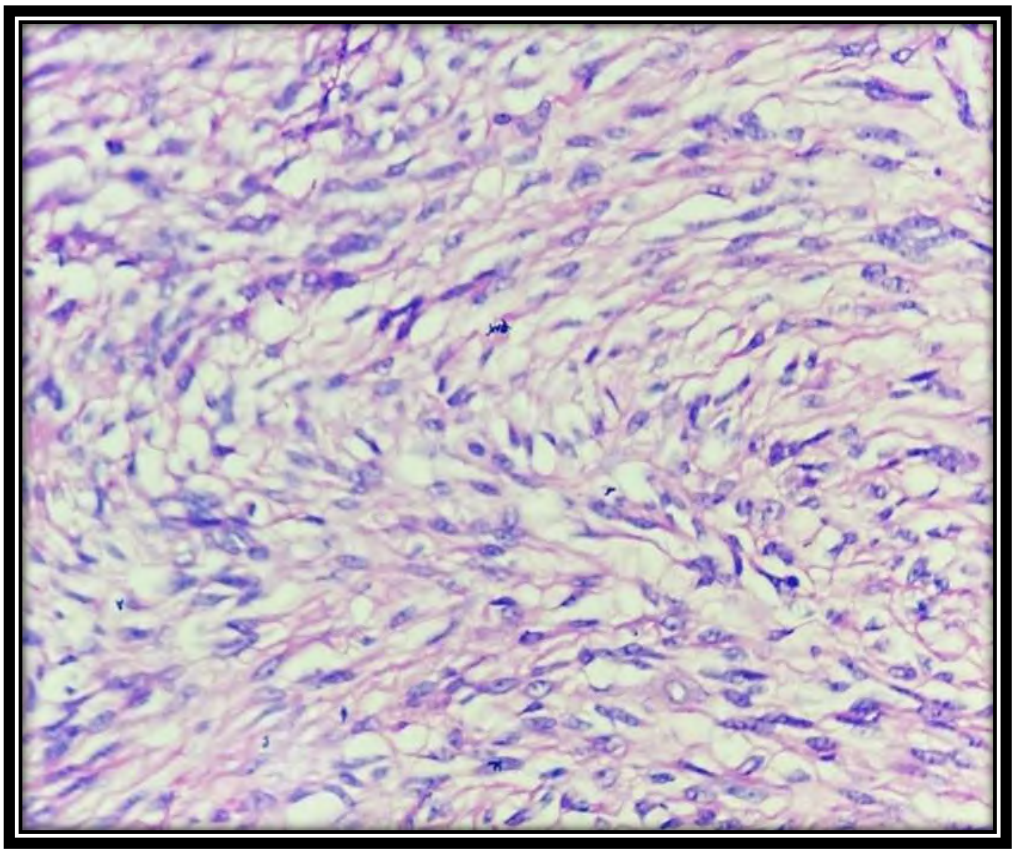
Picture 64- Photomicrograph of showing metastatic lobular breast carcinoma to ovaries showing diffuse nuclear PR positivity (H&E, 100X)



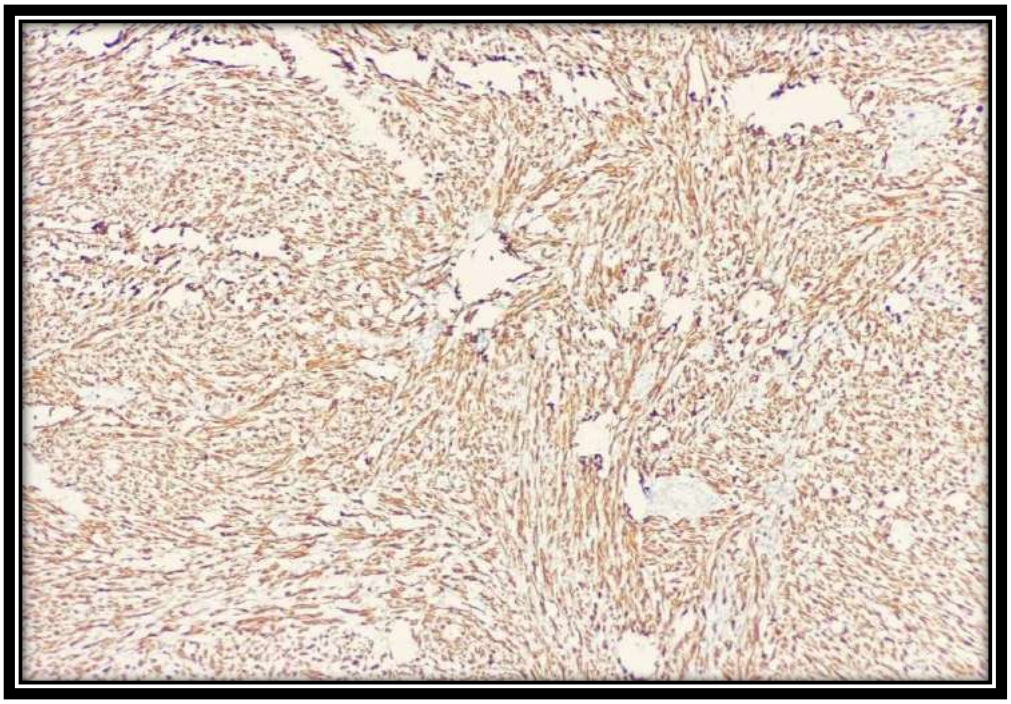
Picture 65- Photomicrograph of showing metastatic lobular breast carcinoma to ovaries showing E cadherin negativity (H&E, 100X)



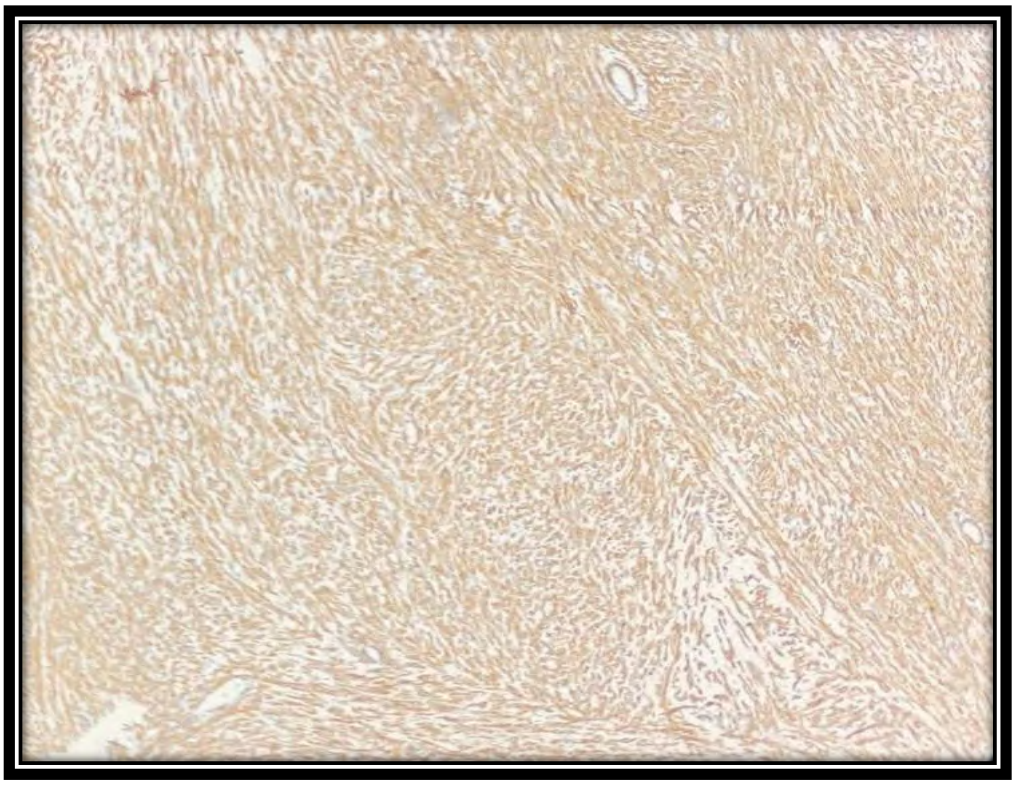
Picture 66- Photomicrograph of metastatic lobular breast carcinoma to ovary showing diffuse nuclear GATA 3 positivity (IHC, 100X)



Picture 67- Photomicrograph of leiomyoma showing intersecting fascicles of spindle shaped tumour cells (H&E, 400X)



Picture 68- Photomicrograph of leiomyoma showing diffuse cytoplasmic Desmin positivity (IHC, 400X)



Picture 69- Photomicrograph of leiomyoma showing diffuse cytoplasmic SMA positivity (IHC, 400X)

Picture 70- Photomicrograph of leiomyoma showing Inhibin negativity (IHC, 400X)

PROFORMA

Sr. No. _____

Name Age/Sex

MRD No. Date

Histopath No. IHC No.

Address

Brief history:

Clinical History

Other (specify):

Past history

Personal history

Family history

- Of any cancer
- Hereditary breast/ovarian cancer
- Lynch syndrome

Reproductive history

Menstrual history

Previous treatment history(surgery/chemotherapy/radiotherapy), if any

General physical examination:

Pallor Icterus Cyanosis Clubbing

Abdomonal examination:

Hepatomegaly Splenomegaly Free fluid

Investigations:

Haemogram

Urine routine

Liver function tests

Renal function tests

Biochemical/Serological markers

- CA-125
- CEA
- AFP
- LDH

Radiological findings:

- USG findings
- CT scan findings
- MRI findings
- PET scan findings

Ancillary Studies

- BRCA1 mutation testing, if any:
- BRCA2 mutation testing, if any:
- DNA mismatch repair enzyme studies, if any:

Gross examination

Type of specimen:

- Trucut / incisional biopsies from ovary/ovaries
- Excisional biopsies/specimen

Total hysterectomy and bilateral salpingo-oophorectomy
Bilateral salpingo-oophorectomy
Right salpingo-oophorectomy
Left salpingo-oophorectomy
Salpingo-oophorectomy, side not specified
Right oophorectomy
Left oophorectomy
Oophorectomy, side not specified
Other (specify): _____

Description of the gross (including site and external features)

Specimen integrity

Specimen Integrity of Right Ovary

- Capsule intact
- Capsule ruptured
- Fragmented
- Other (specify):

Specimen Integrity of Left Ovary

- Capsule intact
- Capsule ruptured
- Fragmented
- Other (specify):

Specimen Integrity of Right Fallopian Tube

- Serosa intact
- Serosa ruptured
- Fragmented
- Other (specify):

Specimen Integrity of Left Fallopian Tube

- Serosa intact
- Serosa ruptured
- Fragmented
- Other (specify):

Tumour site

- Right ovary
- Left ovary
- Bilateral ovaries
- Ovary, laterality cannot be determined:
- Right fallopian tube
- Left fallopian tube
- Bilateral fallopian tubes
- Fallopian tube, laterality cannot be determined:
- Right tubo-ovarian
- Left tubo-ovarian
- Bilateral tubo-ovarian
- Tubo-ovarian, laterality cannot be determined:
- Primary peritoneum
- Other:

Ovarian Surface Involvement

- Present Specify laterality:
- Absent
- Cannot be determined:

Fallopian Tube Surface Involvement

- Present Specify laterality:
- Absent
- Cannot be determined:

Size

- Tumor Size (in centimeters)

Cut section

- Cystic
- Solid
- Unilocular
- Multilocular
- Contents with consistency- serous/mucinous/hemorrhagic
- Colour
- Fibrosis
- Calcification
- Any other

Implants

- Not sampled
- Not identified
- Present (specify sites)

Lymph nodes (if present in the specimen)

- Involved
- Uninvolved
- Cannot comment

Microscopic examination:

WHO Grading System

G1: Well differentiated

G2: Moderately differentiated

G3: Poorly differentiated

GX: Cannot be assessed

Two-Tier Grading System

Low grade

High grade

Other (specify):

Not applicable

Provisional histopathological diagnosis:

IHC Markers: Cytoplasmic Nuclear Membranous Intensity Focal Diffuse

ER

PR

CK7

CK20

Pax-8

HMWCK

EMA

CEA

CA 125

WT1

Beta- catenin

Vimentin

GATA 3

p53

Napsin A

Inhibin

Calretinin

SF-1

FOXL2

PLAP

CD117

AFP

Glypican-3

hCG

SALL4

Chromogranin

Synaptophysin

NSE

CD56

CD30

P16

Rb1

Ki-67

MIB-1

SATB2

CDX2

Any other

Immunohistochemical findings:

Final histopathological findings:

Sr. No	NAME	AGE/SEX	MRD.NO.	HISTOPATH.NO.	IHC.NO.	BRIEF HISTORY	GPE PICC	HEPATOMEGALY	SPLENOMEGALY	ASCITES	HEMOGRAM	URINE ROUTINELFTS	LFTS	RFTS	CA-125	CEA	AFP	LDH	RADIOLOGY	ANCILLARY STUDIES	GROSS-TYPE OF SPECIMEN
1	KK	33F	967890	20-6625	773/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	14074	462	NA	ND	TRUCUT BX RIGHT OVARY
2	VK	15F	1019118	21-890	104/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	2401	686	NA	ND	TRUCUT BX ADENEXAL MASS
3	VB	28F	1211428	21-11532	1355/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	2522	NA	NA	ND	RIGHT ADENEXAL MASS
4	KR	69F	1274194	22-2954	454/22	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	RIGHT OVARIAN MASS
5	MK	51F	1172631	21-9918	1108/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	OUTSIDE BLOCKS
6	AK	50F	1162821	21-8518	1049/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	6.7	1.05	NA	NA	NA	ND	HYSTERECTOMY SPECIMEN WITH B/L ADENEXA, OMENTUM B/L PELVIC LN
7	K	38F	1258270	22-1598	254/22	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	RIGHT OVARIAN CYST
8	NM	63F	1059192	21-2685,2696	316/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	LEFT ADENEXA TAH RIGHT ADENEXA OMENTUM RIGHT LEFT PELVIC LN
9	NKB	57F	916136	20-3001	286/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	95.7	0.66	1.73	NA	NA	ND	RIGHT OVARIAN MASS WITH HYSTERECTOMY SPECIMEN
10	NK	31F	977800	20-7317	865/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TRUCUT BX ADENEXAL MASS
11	S	51F	977400	20-7162	861/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TRUCUT BX-RIGHT ADENEXA
12	BK	45F	1251104	22-1284	148/22	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	OUTSIDE BLOCKS
13	IK	52F	1252525	22-1207	194/22	KCO CARCINOMA BRE	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TRUCUT BX RIGHT ADENEXA
14	MV	47F	885301	20-9028	23/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	1989.8	NA	NA	NA	NA	ND	TRUCUT BX - ADENEXAL MASS
15	S	56F	964596	20-6757	775/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TRUCUT BX LEFT ADENEXA
16	US	67F	474651	21-11904	1321/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	88.9	NA	4.59	272	NA	ND	TRUCUT BX ADENEXAL MASS

DESCRIPTION OF GROSS	SPECIMEN INTEGRITY-RIGHT OVARY	SPECIMEN INTEGRITY-LEFT OVARY	SPECIMEN INTEGRITY - RIGHT FT	SPECIMEN INTEGRITY-LEFT FT	TUMOUR SITE	OVARIAN SURFACE INVOLVEMENT	FT SURFACE INVOLVEMENT	TUMOUR SIZE	CUT SECTION	IMPLANTS	L.N.
TRUCUT BX MEASURING 1.1CM	NA	NA	NA	NA	RIGHT OVARY	NA	NA	NA	NA	NA	NA
TRUCUT BX MEASURING 1 CM	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
MEASURE 6X4X3.2CM	INTACT	NA	NA	NA	RIGHT ADENAXA	ABSENT	NA	5X4X3.5CM	SOLID CYSTIC	NA	NA
RIGHT OVARIAN MASS MEASURING 22X15X9CM.	INTACT	NA	NA	NA	RIGHT OVARY	ABSENT	NA	22X15X9CM	SOLID AND MULTICYSTIC	NA	NA
NA	NA	NA	NA	NA	LEFT AND RIGHT OVARIAN MASS FT	NA	NA	NA	NA	NA	NA
LEFT OVARY MEASURES 5.5X4.5X3CM UTERUS TM MEASURES 6X3.5X3CM >1/2 OF MYOMETRIUM, IN FUNDUS BODY ISTHMUS AND ENDOCERVICAL	NA	INTACT	NA	NA	LEFT OVARY AND UTERUS	ABSENT	NA	5.5X4.5X3CM-LEFT OVARY 6X3.5X3CM	SOLID AND CYSTIC.SEROUS FLUID DRAINED OUT	ABSENT	ABSENT
MEASURES 4X4X2CM		INTACT	NA	NA	NA	ABSENT	NA	4X3X2CM	OLID CYSTIC	NA	NA
RIGHT OVARY 4X4X4CM LEFT OVARY 4.4X4X3CM	INTACT	INTACT	INTACT	INTACT	LEFT RIGHT OVARY	ABSENT	ABSENT	4X4X3CM	SOLID CYSTIC	ABSENT	3/8 RIGHT PELVIC LN 2/8
RECEIVED A RIGHT OVARIAN MASS WITH FT ATTACHED MEASURING	INTACT	INTACT	INTACT	INTACT	RIGHT OVARY	ABSENT	ABSENT	8X5X5CM	SOLID AND MULTI CYSTIC. MUCINOUS FLUID DRAINED	ABSENT	NA
TRUCUT BX MEASURING 1 CM IN LENGTH	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
2 TRUCUT BX STRIPS MEASURING 0.2 CM IN LENGTH EACH	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
NA	NA	NA	NA	NA	B/L ovarian masses	NA	NA	NA	NA	NA	NA
TRUCUT BX MEASURING 0.4&1 CM	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
ADENEXAL MASS- TRUCUT BX MEASURING 0.8CM IN LENGTH	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
TWO TRUCUT BX STRIPS MEASURING 0.5CM IN LENGTH EACH	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

MICROSCOPIC EXAMINATION	WHO GRADING	TWO TIER GRADING	PROVISIONAL HISTOPATHOLOGICAL DIAGNOSIS	ER	PR	CK7	CK20	PAX-8	HMWCK	EMA	CEA	CA125	WT1	BETA-CATENIN	VIMENTIN	GATA3	p53	NAPSIN A	INHIBIN
EXTENSIVE AREAS OF NECROSIS WITH DC FEW CELLS NODULES SHEETS OF CELLS ROUND NUCLEI MODERATE VACUOLATED CYTOPLASM	NG	NA	GERM CELL TUMOUR POSSIBLY YOLK SAC TUMOUR	N	ND	N	N	N	ND	ND	ND	ND	N	ND	ND	ND	ND	ND	ND
TM PRESENT	NG	NA	GERM CELL TUMOUR POSSIBLY YOLK SAC TUMOUR	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
CELLULAR TM IN SHEETS RETICULAR PATTERN WITH CYSTIC CHANGE IX TM CELLS MOD TO MARKED NP VN PN MOD CYTOPLASM. ATYPICAL MF WITH INTRACYTOPLASMIC HYALINE GLOBULES FOCAL MYXOID AREAS NO CYTO/SYNTIOTROPHOBLAST/CAPSULAR BRECAH SEEN	NG	NA	GERM CELL TUMOUR POSSIBLY YOLK SAC TUMOUR	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
CELLULAR TM IN SHEETS HAVING VN ICN MOD CYTOPLASM. INTERSPERSED ARE SEEN FEW DELICATE BV. FEW NUCLEAR GROOVES SEEN. RETICULIN STAIN HIGHLIGHTS	NG	NA	SEX CORD STROMAL TUMOUR	P(DIFFUSE)	N	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P
TM ARRANGED IN NESTS SEPARATED BY THIN FIBROVASCULAR SEPTA TRABECULAR ARRANGEMENT OCCASIONAL TUBULE FORMATION. IX TM CELLS ROUND TO OVAL VN ICN MOD CYTOPLASM OCCASIONAL MF SEEN.FT SHOWS SIMILAR TM.	NG	NA	?SEX CORD STROMAL TUMOURS ??METASTASIS	P	P	ND	N	N	ND	N	N	ND	N	ND	P	N	ND	ND	P(FOCAL)
CELLULAR TM IN SHEETS AND GLANDULAR CONFIGURATION.IX TM CELLS VN PN AND MOD CYTOPLASM	NG	NA	ADENOCARCINOMA	P(FOCAL)	P(FOC	ND	ND	P	ND	ND	ND	ND	N	ND	P(FOCAL)	ND	WILD TYPE	ND	ND
CYSTS LINED BY TALL COLUMNAR MUCIN SECRETING CELLS . FOCAL BASALLY LOCATED NUCLEI WITH CILIA NO HYPERCHROMASIA NS INVASION SEEN	NG	NA	BENIGN EPITHELIAL TUMOUR WITH SEROMICINOUS DIFFERENTION	P	ND	POSIT	NEGAT	POSITIV	ND	ND	ND	ND	POSITIVE IN C	ND	ND	ND	ND	ND	ND
TM IN MULTIPLE CYSTS LINED BY TALL COLUMNAR MUCIN SECRETING EPITHELIUM IN PAPILLAE FOCAL GLANDS IN STROMA CREATING LABYRINTH APPEARANCE. MILD NP	NG	NA	MUCINOUS CARCINOMA	ND	ND	P	P	N	ND	ND	ND	ND	ND	ND	ND	ND	P(FOCAL)	ND	ND
NUMEROUS CYSTS LINED BY TALL COULUMNAR MUCIN SECRETING EPITHELIUM FOCALLY FORMING GLANDS AND PAPILLAE. CELLS SHOW NS MOD NP PN MOD	NG	NA	MUCINOUS CARCINOMA	ND	ND	P	P	ND	ND	ND	ND	ND	N	ND	ND	ND	P(FOCAL)	N	ND
OVARIAN STROMA WITH LINING OS TALL COLUMNAR MUCIN SECRETING EPITHELIUM NUCLEAR STRATIFICATION>4 LAYERS FOCI EXHIBITING CONFLUENT GLANDS HAVING PAPILLARY PROJECTIONS WITH MINMAL INTERVENING STROMA-INVASIVE COMPONENT	NG	NA	MUCINOUS CARCINOMA	ND	ND	P	P	N	ND	ND	ND	ND	N	ND	ND	ND	P(FOCAL)	ND	ND
PRESENCE OF A CELLULAR TUMOUR WITH TUMOUR CELLS ARRANGED IN GLANDS AND NESTS. IX TM CELLS EXHIBIT NUCLEAR HYPERCHROMASIA AND STRATIFICATION. OCCASIONAL MITOSIS SEEN.	NG	NA	METASTATIC ADENOCARCINOMATOUS DEPOSITS	N	N	ND	ND	ND	ND	ND	ND	ND	N	ND	ND	ND	ND	ND	ND
FC TISSUE INFILTRATED BYTM CELLS IN SINGLE FILE PATTERN CORDS IX TM CELLS MONOMORPHIC ROUND NUCLEI MOD CYTOPLASM	NG		ADENOCARCINOMA	P	P	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P	ND	ND	ND
POOLS OF EXTRA CELLULAR MUCIN WITHIN WHICH ARE SEEN TINY CLUSTERS TM CELLS ECCENTERIC HN MOD CYTOPLASM OCCASIONAL ACINAR CONFIGURATION SEEN	NG		ADENOCARCINOMA	P	P	ND	ND	P	ND	ND	ND	ND	ND	ND	ND	P	ND	ND	ND
TM ARRANGED IN GLANDULAR CONFIGURATION AND SHEETS. IX TM CELLS HAVE VN PN AND MOD CYTOPLASM	NG	NA	METASTATIC ADENOCARCINOMATOUS DEPOSITS	N	ND	P	N	N	ND	ND	P	ND	N	ND	ND	ND	ND	ND	ND
CELLULAR TM WITH TM CELLS ARRANGED IN GLANDS AND NESTS HAVING VN AND MODERATE TO ABUNDANT CYTOPLASM. FOCI OG HEMORRHAGE AND NECROSIS.	MODERATELY	NA	METASTATIC ADENOCARCINOMATOUS DEPOSITS	N	ND	P	N	N	ND	ND	ND	ND	N	ND	ND	ND	ND	ND	ND
CELLULAR TM TUBULAR AND GLANDULAR CONFIGURATION FOCAL SOLID PATTERN SEPARATED BY OVARIAN STROMA. IX TM CELLS VN ICN MOD CYTOPLASM FOCAL CLEARING	NG	NA	NA	N	N	P(FOC	P(FOCA	P(WEAK	ND	ND	ND	ND	N	ND	P(FOCAL)	P	N	ND	ND

CALRETININ	SF-1	FOXL2	PLAP	CD117	AFP	GLYPICAN-3	hCG	SALL4	CHROMOGRANIN	SYNAPTOPHYSIN	NSE	CD56	CD30	P16	Rb1	Ki-67	MIB-1	SATB2	CDX2	OTHERS	IHC FINDINGS	FINAL HISTOPATHOLOGICAL DIAGNOSIS
ND	ND	ND	ND	ND	ND	P	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	YOLK SAC TUMOUR	YOLK SAC TUMOUR
ND	ND	ND	N	N	P(FOCAL)	P	ND	ND	ND	ND	ND	ND	N	ND	ND	ND	ND	ND	ND	ND	YOLK SAC TUMOUR	YOLK SAC TUMOUR
ND	ND	ND	ND	ND	P(FOCAL)	P	ND	P	ND	ND	ND	ND	N	ND	ND	ND	ND	ND	ND	OCT4 NEGATIVE GLYPICAN 3 POSITIVE	YOLK SAC TUMOUR	YOLK SAC TUMOUR
N	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	THECOMA	THECOMA
ND	ND	ND	ND	ND	ND	ND	ND	N	ND	ND	ND	ND	ND	ND	ND	ND	ND	N	ND	MELAN A NEGATIVE TTF1 NEGATIVE CK	SERTOLI CELL TUMOUR	SERTOLI CELL TUMOUR
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P	ND	ND	ND	ND	ND	ND	SEROUS CARCINOMA-OVARYA AND UTERUS	METASTATIC ENDOMETRIAL SEROUS CARCINOMA TO OVARY
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	N	ND	SEROMUCINOUS CYSTADENOMA	SEROMUCINOUS CYSTADENOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	FOCAL P	ND	MUCINOUS CARCINOMA WITH	MUCINOUS CARCINOMA WITH INTESTINAL
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	N	ND	MUCINOUS CARCINOMA	MUCINOUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	N	ND	MUCINOUS CARCINOMA	MUCINOUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P	ND	ND	ND	ND	ND	ND	METASTATIC ENDOCERVICAL ADENOCARCINOMATOUS DEPOSITS HPV RELATED	METASTATIC ENDOCERVICAL ADENOCARCINOMATOUS DEPOSITS HPV RELATED
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	8%	ND	ND	HER2NEU NEGATIVE	METASTATIC DEPOSITS LOBULAR CARCINOMA BREAST	METASTATIC DEPOSITS LOBULAR CARCINOMA BREAST
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	HER2NEU 1+	METASTATIC CARCINOMATOUS	METASTATIC CARCINOMATOUS
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P	ND	METASTATIC ADENOCARCINOMATO	METASTATIC ADENOCARCINOMATOUS
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	N	P	ND	METASTATIC ADENOCARCINOMATO	METASTATIC ADENOCARCINOMATOUS
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	N	TTF1 NEGATIVE AR FOCAL WEAK POSITIVE CK POSITIVE	MESONEPHRIC LIKE ADENOCARCINOMA	MESONEPHRIC LIKE ADENOCARCINOMA

17	D	26F	922066	20-3470	303/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	1705.9	0.89	NA	NA	NA	ND	TRUCUT BIOPSY OVARIAN MASS
18	MK	69F	225056	20-6627	756/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	565.6	6.9	NA	NA	NA	ND	TRUCUT BIOPSY RIGHT ADNEXAL MASS
19	KR	47F	927625	20-6383	716/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	149.1	1.95	NA	NA	NA	ND	TRUCUT BIOPSY-PELVIS
20	JD	46F	1048711	21-3410	460/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TAH BSO
21	TD	50F	1113566	21-4243	574/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	B/L ADENEXA
22	ND	45F	1198819	21-10315	1247/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	10.8	NA	NA	NA	NA	ND	TAH BSO OMENTAL BX PERITONEAL BX
23	DR	43F	972577	20-8537	1025/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	19.55	NA	1.52	NA	NA	ND	TOTAL HYSTERECTOMY AND BILATERAL SALPINGO-OOPORECTOMY WITH LYMPH NODES
24	TD	66F	1179481	21-9033	1085/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	RIGHT OVARIAN CYST
25	SK	63F	923251	21-1942	315/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	784.5	NA	NA	NA	NA	ND	TRUCUT BX RIGHT ADENEXAL MASS
26	SKD	62F	923251	20-3544	302/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TRUCUT BX ADENEXAL MASS
27	SB	54F	253124	21-8148	989/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	126	NA	2.6	NA	NA	ND	HYSTERECTOMY WITH B/L ADENEXA B/L PELVIC LN
28	KK	58F	777286	22-619	88/22	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	55.8	NA	NA	NA	NA	ND	TRUCUT BX RIGHT ADENEXA
29	PD	62F	1157571	21-11707	1299/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	24224	0.2	NA	NA	NA	ND	TRUCUT BX ADENEXAL MASS
30	KK	48F	1022387	21-1095	133/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	255.9	1.22	2.3	NA	NA	ND	TRUCUT BIOPSY
31	DD	67F	1006078	20-9119	49/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	LEFT SALPINGO-OOPHORECTOMY AND

RECEIVED 2 TRUCUT BIOPSY STRIPS MEASURING 0.3 AND 0.4 cm IN LENGTH	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
MULTIPLE TRUCUT BIOPSY STRIPS RANGING IN LENGTH FROM 0.1-0.2 cm.	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
2 TRUCUT BIOPSY STRIPS MEASURING 1.4 AND 0.8 cms IN LENGTH	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
RIGHT OVARY MEASURES 7X4.5X3.5CM.	RIGHT OVARY	NA	NA	NA	RIGHT OVARY	ABSENT	NA	7X4.5X3.5CM	SOLID AND CYSTIC.CYST MEASURED 4.5 CM IN DIAMETER AND FILLED WITH MUCOID MATERIAL. PAPILLARY EXCRESCENCES NOTED.	NA	NA
RIGHT OVARY MEASURES 5X5X3CM LEFT OVARY MEASURES4X3.8X3CM	INTACT	INTACT	NA	NA	BL ADENEXA	ABSENT	NA	RIGHT OVARY 5X4X3CM LEFT OVARY 4X3.8X3 CM	SOLID AND CYSTIC WITH MUCOID AREAS	NA	NA
LEFT OVARY 5X4X3CM	NA	INTACT	NA	INTACT	LEFT ADENEXAL MASS	ABSENT	NA	4X4X3CM	SOLID	NA	NA
B/L TUBOOVARIAN MASS	INTACT	INTACT	NA	NA	B/L TUBOOVARIAN MASS	ABSENT	NA	RIGHT TO MASS- 11X9X6CM LEFT TO MASS -4X2.5X1CM	SOLID AND CYSTIC	ABSENT	ABSENT
RECEIVED AN OVARIAN MASS MEASURING 15X12X5CM.	INTACT	NA	NA	NA	RIGHT OVARIAN CYST	ABSENT	NA	9X6X5CM	SOLID AND MULTICYSTIC WITH FLUID DRAINED OUT	NA	NA
ADENEXAL MASS TRUCUT BX MEASURING 2 CM IN LENGTH	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
TRUCUT BX MEASURING0.3 AND 0.4 CM	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
B/L OVARIES	RIGHT OVARY	ABSENT	ABSENT	NA	BL OVARIES	ABSENT	NA	RIGHT OVARY-12X9X4CM LEFT OVARY-11X8X5CM	RIGHT OVARY-UNILOCULAR CYST WITH PAPILLARY EXCRESCENCES, LEFT OVARY-MULTILOCULAR WITH MUCOID FILLED CYSTS	PRESENT	ABSENT
RECEIVED ONE TRUCUT BX STRIP MEASURING 0.4 CM IN LENGTH	NA	NA	NA	NA	RIGHT ADENAXA	NA	NA	NA	NA	NA	NA
RECEIVED MULTIPLE TRUCUT BX STRIPS RANGING 0.2 TO 1 CM	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
MULTIPLE TRUCUT BIOPSY STRIPS RANGING IN LENGTH FROM 0.6-1.2 cm.	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
RECEIVED LEFT ADNEXA AND RIGHT OVARY. LEFT OVARY MEASURES 6.5X5X3	INTACT	INTACT	NA	NA	RIGHT AND LEFT OVARY	ABSENT	ABSENT	LEFT-3.5X3X2cm RIGHT-3X3X1.8	SOLID AND CYSTIC	NA	NA

PRESENCE OF A CELLULAR TUMOUR WITH TUMOUR CELLS ARRANGED IN PAPILLARY CONFIGURATION WHICH ARE LINED BY CUBOIDAL CELLS HAVING FINE NUCLEAR CHROMATIN ,ICONSPICOUS NUCLEOLI AND MODERATE CYTOPLASM.FOCI OF DYSTROPHIC CALCIFICATION NOTED.	NG	LOW GRADE	NG	P	ND	P	N	ND	ND	ND	ND	ND	P	ND	ND	ND	P(DIFFUSE)	ND	ND
A CELLULAR TUMOUR ARRANGED IN PAPILLAE AND GLANDS.INDIVIDUAL TUMOUR CELLS HAVE HYPERCHROMATIC NUCLEI WITH MODERATE AMOUNT OF CYTOPLASM AND EXHIBIT MILD NUCLEAR PLEOMORPHISM. PSAMMOMA BODIES NOTED.	NG	LOW GRADE	NG	P	ND	ND	ND	P	ND	ND	ND	ND	P	ND	ND	ND	P(FOCAL)	ND	ND
CELLULAR TUMOUR WITH CELLS ARRANGED IN NESTS , GLANDS AND PAPILLAE. INDIVIDUAL TUMOUR CELLS HAVE PLEOMORPHIC VESICULAR NUCLEI, PROMINENT NUCLEOLI AND MODERATE CYTOPLASM. PSAMMOMA BODIES ALSO SEEN.	NG	LOW GRADE	NG	P	ND	ND	ND	P	ND	ND	ND	ND	P	ND	ND	ND	P(FOCAL)	ND	ND
TM IN NESTS AND ARBORIZING PAPILLAE ROUND TO OVAK VN PN MOD CYTOPLASM. HOBNAILING SEEN OCCASIONAL FOCUS OF INVASION SEEN	NG	LOW GRADE	ADENOCARCINOMA	P	P	ND	ND	ND	ND	ND	ND	ND	P	ND	ND	ND	P(FOCAL)	ND	ND
CELLULAR TM ARRANGED IN GLANDULAR CONFIGURATION IX TM CELLS VN PN AND MOD AMOUNT OF VACOULATED CYTOPLASM	NG	NA	ADENOCARCINOMA	ND	ND	N	P	N	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
TM CELLS OF INTERSECTING FASICLES OF BLAND SPINDLE CELLS WITH CYSTIC CHANGE ALONG WITH FOCAL AREAS WITH HYALINISATION	NG	NA	NA	ND	ND	ND	ND	ND	ND	ND	ND	ND	P	ND	ND	ND	ND	ND	N
WELL CIRCUMSCRIBED NODULES WITH TUMOUR ARRANGED IN FASICLES AROUND VASCULAR CHANNELS. IX TM CELLS OVAL TO ELONGED VN WITH MOD CYTOPLASM. OCCASIONAL MITOSIS SEEN. TM PRESENT ON LYMPHOVASULAR CHANNELS.	NG	NA	SPINDLE CELL NEOPLASM	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
CELLULAR TM IN GLANDS TUBULES PAPILLAE CRIBRIFORM AND SOLID PATTERN. TM CELLS HAVE PLEOMORPHIC NUCLEI VN PN AND MODERATE CYTOPLASM. LARGE AREAS OF NECROSIS WITH STROMAL INVASION SEEN.	NG	HIGH GRADE	ADENOCARCINOMA	P(DIFFUSE)	P(FO	ND	N	ND	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	NULL	ND	ND
TM ARRANGED IN SHEETS AND GLANDS. UX TM CELLS HAVE VN PN AND MOD CYTOPLASM	NG	HIGH GRADE	ADENOCARCINOMA	N	P(FO	ND	ND	ND	ND	ND	ND	ND	N	ND	ND	ND	P	P(FOCAL)	ND
TM IN NESTS AD GLANDS MARKED NP HN MOD CYTOPLASM NECROSIS	NG	HIGH GRADE	ADENOCARCINOMA	N	P(FO	ND	ND	ND	ND	ND	ND	ND	N	ND	ND	ND	P	P(FOCAL)	ND
CELLULAR TM IN SHEETS,PAPILLAE,FE GLANDS AND CRIBRIFORM PATTERN. IX TMM CELLS VN PN AND MOD CYTOPLASM. ATYPICAL MF SEEN. CAPSULAR INVASION SEEN.	NG	HIGH GRADE	ADENOCARCINOMA	P(DIFFUSE)	P(FO	P	N	ND	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
TM CELLS ARRANGED IN NESTS,SHEETS AND FOCAL PAPILLAE. IX TM CELLS HAVE PLEOMORPHIC VN PN AND MOD CYTOPLASM.	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	ND	ND	P	N	P	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
TM CELLS ARRANGED IN GLANDS, PAPILLAE, SOLID NESTS. IX TM CELLS HAVE HIGH NC RATIO ANISONUCLEOSIS, VC, PN AND ABUNDANT CYTOPLASM. FOCI OF DC NOTED	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	P (DIFFUSE)	P(FO	ND	N	P	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
CELLULAR TUMOUR WITH CELLS ARRANGED IN NESTS , GLANDS AND PAPILLAE. INDIVIDUAL TUMOUR CELLS HAVE PLEOMORPHIC VESICULAR NUCLEI, PROMINENT NUCLEOLI AND MODERATE CYTOPLASM.	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	ND	P(FO	P	N	P	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
SECTIONS SHOW A CELLULAR TUMOUR WITH CELLS ARRANGED IN NESTS AND	MODERATE	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE	ND	N	ND	ND	ND	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND

ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	25%	ND	ND	ND	LOW GRADE SEROUS CARCINOMA	LOW GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	LOW GRADE SEROUS CARCINOMA	LOW GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	30%	ND	ND	ND	LOW GRADE SEROUS CARCINOMA	LOW GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	LOW GRADE SEROUS CARCINOMA	LOW GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P	ND	LOW GRADE APPENDICEAL MUCINOUS NEOPLASM METASTATIS TO OVARIES	LOW GRADE APPENDICEAL MUCINOUS NEOPLASM METASTATIS TO OVARIES
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	SMA POSITIVE DESMIN POSTIVE	LEIOMYOMA	LEIOMYOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	SMA POSITIVE DESMIN POSITIVE CD10 POSITIVE CD34 POSITIVE	INTRAVENOUS LEIOMYOMATOSIS	INTRAVENOUS LEIOMYOMATOSIS
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(DIFF	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(DIFF	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA LIKELY	HIGH GRADE SEROUS CARCINOMA LIKELY
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(DIFF	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA LIKELY ENDOMETRIAL IN ORIGIN WITH	HIGH GRADE SEROUS CARCINOMA LIKELY ENDOMETRIAL IN ORIGIN WITH METASTATIC
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	N	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	60%	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS	HIGH GRADE SEROUS

32	BR	53F	1004890	21-28	46/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	54.5	NA	NA	NA	NA	ND	EXCISIONAL BIOPSY
33	KK	57F	967627	21-2621	413/21	OUTSIDE BLOCKS	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	15.9	NA	NA	NA	NA	ND	OUTSIDE BLOCKS
34	K	54F	65016	21-3383	408/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	5160	NA	NA	NA	NA	ND	TRUCUT BX ADENEXAL MASS
35	SD	47F	1120217	21-4592	585/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	1.25	4.38	NA	NA	NA	ND	TRUCUT BX ADENXAL LESION
36	NK	53F	4047	22-1400	176/22	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TRUCUT BX ADENEXAL MASS
37	SK	51F	1019654	22-1184	136/22	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	576	NA	NA	NA	NA	ND	TRUCUT BX LEFT ADENEXA
38	SK	50F	71881	22-670	120/22	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	2118	0.6	NA	NA	NA	ND	HYSTERECTOMY WITH B/L OVARIAN MASSES B/L FT AND OMENTUM
39	VD	64F	1206950	21-10862	1260/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	1.25	NA	NA	NA	ND	B/L ADENEXA
40	PD	53F	1147309	21-10121	1165/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	167	0.9	3.22	214	NA	ND	HYSTERECTOMY SPECIMEN WITH B/L FT, OVARIAN MASS, OMENTUM AND B/L PELVIC LN
41	MK	37F	1184965	21-9383	127/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	197	NA	2.1	NA	NA	ND	LEFT TUBOOVARIAN MASS
42	SK	64F	1149959	21-7074	874/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	232	NA	NA	NA	NA	ND	HYSTERECTOMY SPECIMEN WITH B/L ADENEXA, B/L PELVIC LN
43	SK	71F	115361	21-7454	866/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TRUCUT BX OVARIAN MASS
44	RS	60F	1141839	21-6374	763/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	191	0.8	NA	152	NA	ND	TRUCUT BX PELVIC MASS
45	KR	74F	1124045	21-4941	628/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	5160	1.52	5.94	611	NA	ND	TRUCUT BX-PELVIC MASS
46	MD	65F	999483	21-8686	22/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	263	4.28	2.17	NA	NA	ND	HYSTERECTOMY WITH B/L TUBE AND ONE SIDED TUBOOVARIAN MASS AND OTHER SIDED OVARY AND LEFT ILIAC
47	S K	57F	280193	21-6733	799/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	411	NA	NA	NA	NA	ND	HYSTERECTOMY SPECIMEN WITH /L ADENEXA OMENTUM AND LN
48	RS	22F	939330	20-4976	544/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	1.97	287	NA	ND	TRUCUT BX PELVIC MASS

RECEIVED A TUBOOVARIAN MASS MEASURING 7X5X4 cm	PAPILLARY EX	NA	NA	NA	RIGHT TUBO OVARIAN MASS	PRESENT	NA	4X3X2.6cm	SOLID AND CYSTIC	PRESENT(UM	NA
NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
RECEIVED MULTIPLE TRUCUT BX STRIPS RANGING IN LENGTH FROM 0.4 TO 0.8 CM	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
RECEIVED TRUCUT BX STRIPS RANGING IN LENGTH FROM 0.6 TO 1 CM	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
RECEIVED MULTIPLE TRUCUT BX STRIPS RANGING IN LENGTH FROM 0.2 TO 0.3 CM	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
RECEIVED TRUCUT BX STRIPS RANGING 0.8 TO 1.2 CM IN LENGTH	NA	NA	NA	NA	LEFT ADENEXA	NA	NA	NA	NA	NA	NA
RIGHT SIDED OVARIAN MASS MEASURES 30X22X16CM. LEFT SIDED OVARIAN MASS MEASURES 12X10X3CM.	INTACT	INTACT	INTACT	INTACT	B/L OVARIES	ABSENT	ABSENT	RIGHT OVARIAN TUMOUR - 5X3X2CM LEFT OVARIAN TUMOUR MEASURE- 4X3X2.5CM	RIGHT OVARY- SOLID AND MULTICYSTIC PAPILLARY EXCRESENCES NOTED. CLEAR FLUID DRAINED OUT. LEFT OVARY- SOLID AND	PRESENT IN C	NA
LEFT OVARY MEASURES 5.5X5X2CM RIGHT OVARY MEASURES 4.5X3X1.4CM	INTACT	INTACT	INTACT	INTACT	B/L OVARIES	ABSENT	ABSENT	LEFT OVARY- 5X5X2CM RIGHT- 4.5X3X1.4CM	BOTH- SOLID AND CYSTIC	NA	NA
OVARIAN MASS MEASURES 5x4x3cm.	INTACT	INTACT	INTACT	INTACT	LATERALITY NOT CONFIRMED	PAPILLARY EX	ABSENT	5X4X3CM	SOLID	OMENTUM P	RH
RECEIVED A TUBOOVARIAN MASS MEASURING 9X8X6CM.	NA	INTACT	NA	NA	LEFT OVARY	PAPILLARY EX	NA	5.5X5X4CM	SOLID AND MULTICYSTIC. MUCOID MATERIAL DRAINED OUT.	NA	NA
LEFT OVARY	NA	INTACT	NA	NA	LEFT OVARY	ABSENT	NA	5X4.5X3CM	MULTIPLE GREY WHITE YELLOWISH SOLID AREAS	NA	4/14 LEFT PELVIC LN
TRUCUT BX MEASURING 1CM IN LENGTH	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
TRUCUT BX MEASURING 0.5 AND 0.8 CM IN LENGTH	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
TRUCUT BX MEASURING 1CM IN LENGTH	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
TUBOOVARIAN MASS MEASURING 5X5X3CM	INTACT	NA	NA	NA	RIGHT OVARIAN MASS	ABSENT	NA	5X5X3CM	SOLID & CYYSTIC	NA	NA
B/L OVARIES	INTACT	NA	INTACT	NA	B/L OVARIES	ABSENT	NA	ONE SIDED-6X4X1.5CM OTHER SIDED -3X1.5X1 CM	ONE SIDED -SOLID & CYSTIC.BROWNISH FLUID DRAINED OUT. OTHER OVARY - SOLID	NA	NA
TRUCUT BX MEASURING 0.5CM IN LENGTH	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

CELLULAR TUMOUR WITH CELLS ARRANGED IN NESTS AND PAPILLAE. INDIVIDUAL TUMOUR CELLS SHOW MODERATE NP,VN,PN AND MODERATE CYTOPLASM.ATYPICAL MITOSIS AND INVASION IN LP SEEN.	MODERATE	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	ND	P(FO	P(21-2	ND	P(21-27	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)21-2	ND	ND
NA	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
CELLULAR TUMOUR WITH CELLS ARRANGED IN NESTS AND PAPILLAE. INDIVIDUAL TUMOUR CELLS SHOW MODERATE NP,VN,PN AND MODERATE CYTOPLASM.ATYPICAL MITOSIS AND INVASION IN LP SEEN.	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	P(DIFFUSE)	N	P	N	ND	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
CELLULAR TM WITH CELLS ARRANGED IN PAPILLAE AND GLANDS. TM CELLS HAVE HN AND MOD CYTOPLASM	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	P(FOCAL)	ND	ND	ND	P	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
FEW PAPILLAE AND NESTS OF TM CELLS WITH PAPILLAE LINED BY 2-3 LAYERS OF CELLS HAVING OVAL NUCLEI MODERATE ANISOKARYOSIS, FINE CHROMATIN, ICN SCANTY CYTOPLASM	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	P (DIFFUSE)	N	ND	ND	P	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
TM CELLS ARRANGED IN NESTS,SHEETS AND FOCAL PAPILLAE. TM CELLS HAVE PLEOMORPHIC VN PN AND MOD CYTOPLASM. AREAS OF NECROSIS AND MITOSIS SEEN	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	P(DIFFUSE)	N	ND	ND	P	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
B/L OVARIES SHOW A CELLULAR TM IN NESTS PAPILLAE AND CORDS. TM CELLS ARE PLEOMORPHIC HN CN AND MODERATE CYTOPLASM. MITOTIC ACTIVITY NOTED. FOCI OF NECROSISS SEEN	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	P(DIFFUSE)	P(FO	ND	ND	P	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
TM CELLS ARE ARRANGED IN PAPILLAE, GLANDS AND SOLID PAATERN.TM CELLS EXHIBIT MARKED NUCLEAR PLEOMORPHISM VN PN AND MODERATE CYTOPLASM.TM IS INFILTRATING THE UNDERLYING STROMA AND REACHING UPTO OVERLYING CAPSULE.	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	P(DIFFUSE)	P(FO	ND	ND	ND	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	NULL	ND	ND
CELLULAR TM WITH CELLS ARRANGED IN GLANDS AND PAPILLAE. PLEOMORPHIC CELLS VN PN MODERATE CYTOPLASM.LARGE AREAS OF HEMORRHAGE AND PSAMMOMA BODIES NOTED.MANY HSLM AND INFLAMMATORY CELLS SEEN.	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	P(DIFFUSE)	N	ND	N	ND	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
CELLULAR TM IN COMPLEX HIERCHIAL BRANCHING PAPILLAE AND SHEETS. TM CELLS PLEOMORPHIC HYPERCHROMATIC NUCLEI AND MODERATE CYTOPLASM.BRISK MITOSIS NOTED.LYMPHTIC INVASION SEEN. NO VASCULAR INVASION SEEN.	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	P(DIFFUSE)	P	ND	ND	ND	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
TM ARRANGED IN PAPILLARY AND GLANDULAR CONFIGURATION . IX TM CELLS VN PN AND MOD CYTOPLASM	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	P(FOCAL)	ND	ND	ND	P	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
TUMOUR CELLS ARRANGED IN PAPILLAE HAVING VN PN AND MODERATE CYTOPLASM. PSAMMOMA BODIES SEEN	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	P(DIFFUSE)	ND	ND	ND	P	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
EXTENSIVE AREAS OF NECROSIS WITH VIABLE AREAS SHOWING CELLULAR TM ARRANGED IN DIFFUSE SHEETS. IX TM CELLS SHOW MOD NP, VN, PN AND MOD CYTOPLASM	NG	HIGH GRADE	ADENOCARCINOMA	N	N	ND	ND	ND	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
LARGE AREAS OF NECROSIS WITH PRESENCE OF CELLULAR TM WITH HIGH N:C RATIO IREGULAR NUCLEAR CONTOURS AND MOD CYTOPLASM. BIZARRE FORMS SEEN,	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	N	ND	P	N	ND	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	NULL	ND	ND
TUMOUR ARRANGED IN NESTS AND SHEETS. IX TM CELLS VN PN AND MODERATE CYTOPLASM.FOCI OF NECROSIS NOTED.	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	P(DIFFUSE)	ND	P	N	P	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
TM IN GLANDULAR CONFIGURATION. IX TM CELLS PLEOMORPHIC VN PN MOD CYTOPLASM.	NG	HIGH GRADE	ADENOCARCINOMA	P	ND	ND	ND	ND	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
CELLULAR TM ARRAGED IN GLANDS HAVING VN AND MOD CYTOPLASM	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	P(DIFFUSE)	ND	ND	ND	P	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	NULL	ND	ND

ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(DIFF	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	60%	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(DIFF	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(DIFF	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(DIFF	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(DIFF	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(DIFF	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	60%	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	80%	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(DIFF	ND	ND	60%	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA

49	MK	68F	929601	20-4111	393/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TRUCUT BX RIGHT ADENEXA
50	RG	35F	922110	20-3447	292/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	RIGHT OVARIAN CYST
51	KK	60F	898596	20-3627	356/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	4933	0.89	2.11	240	NA	ND	TAH WITH BSO OMENTUM LEFT RIGHT PELVIC LN LEFT AND RIGHT PERITONEUM
52	KK	36F	927605	20-3984	377/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	1105	1.9	NA	1212	NA	ND	TRUCUT BX PELVIC MASS
53	GK	64F	599019	20-6510	770/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	8.6	1.2	NA	NA	NA	ND	LEFT OVARIAN MASS AND LEFT FT
54	RK	47F	1140061	21-6229	792/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	6415	6.78	3.65	NA	NA	ND	TRUCUT BX RIGHT OVARY
55	SR	52F	1167868	21-8255	1019/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TAH BSO LN
56	GK	27F	1142811	21-6438	900/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	RIGHT OVARIAN MASS
57	HK	62F	1229966	22-105	56/22	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TAH BSO OMENTUM B/L LN
58	SM	42F	1137907	21-8243	1155/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TAH BSO B/L ADENEXA
59	KK	46F	971760	20-8768	17/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	26.9	NA	1.93	NA	NA	ND	B/L OVARIES AND LEFT FT
60	M	41F	931228	20-4249	491/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	HYSTERECTOMY WITH B/L OVARIAN MASSES B/L FT AND OMENTUM, RIGHT AND LEFT PELVIC LN
61	JK	52F	1151941	21-7067	884/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TRUCUT BX ADENEXAL MASS
62	S	47F	1206648	21-10650	1244/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TAH BSO OMENTUM B/L PELVIC LN
63	RT	58F	1030637	21-1563	184/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	318	NA	NA	NA	NA	ND	PELVIC MASS
64	AK	52F	1106044	21-6769	856/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	5920	NA	NA	304	NA	ND	RIGHT TUBOOVARIAN MASS
65	V	47F	1045966	21-2261	260/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TRUCUT BX ADENEXAL LESION
66	P	52F	1031279	21-1648	236/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TAH BSO BL PELVIC LNS
67	AK	40F	980693	20-7564	893/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	128.5	1.69	NA	NA	NA	ND	TRUCUT BX ADENEXAL MASS
68	BS	43F	1018125	21-813	137/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	2678	NA	NA	NA	NA	ND	OVARY
69	NK	27F	1007291	21-45	93/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	87.2	NA	1.92	860	NA	ND	RIGHT ADENEXAL MASS OVARY FT OMENTUM RIGHT AND LEFT PELVIC LN LEFT OVARIAN BX
70	A	18F	559460	21-8593	1063/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	RIGHT OVARY FT RIGHT PELVIC AND PARA AORTIC LN RIGHT AND LEFT PERITONEAL BX
71	M	27F	890009	20-1255	158/22	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	RIGHT ADENEXAL MASS
72	RKA	43F	1192541	21-10093	1167/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	139.5	NA	NA	NA	NA	ND	HYSTERECETOMY+B/L FT LEFT OVARY RIGHT OVARIAN MASS OMENTUM RIGHT AND LEFT PELVIC LNS PARA AORTIC LN
73	N	60F	1204666	21-10536	1168/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	2234	0.7	NA	NA	NA	ND	TRUCUT BX ADENEXAL MASS

TRUCUT BX STRIP MEASURING 0.4CM IN LENGTH	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
OVARIAN MASS. CAPSULAR BREECH NOTED.	CAPSULAR BR	INTACT	SEROSA INTA	NA	RIGHT OVARY	PRESENT	ABSENT	16X12X4CM	SOLID AND CYSTIC- PAPILLARY EXCRESENCES	NA	NA
LEFT OVARY & RIGHT OVARY	INTACT	NA	INTACT	NA	B/L OVARIES	ABSENT	NA	RIGHT OVARY-4X2.5X1CM LEFT OVARY-3X2X1CM	BOTH-SOLID	PRESENT-OM	1/6-LEFT PELVIC LN 11/15-RIGHT PELVIC LN
TRUCUT BX MEASURING 0.5CM IN LENGTH	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
OVARIAN MASS MEASURING 7X6X3CM.NO CAPSULAR BREACH	NA	INTACT	NA	NA	LEFT OVARY	ABSENT	NA	7X6X3CM	SOLID AND CYSTIC HEMORRHAGIC FLUIDS	NA	NA
MULTIPLE TRUCUT BX RANGING FROM 0.2-0.4 CM	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
WELL CIRCUMSCRIBED GREY WHITE MASS MEASURING 13X11X8CM.NO RESIDUAL OVARY SEE.	NA	INTACT	NA	INTACT	LEFT OVARY	ABSENT	ABSENT	13X11X8CM	GREY WHITE WITH MUCOID AREAS	ABSENT	ABSENT
RECEIVED A WELL ENCAPSULATED MASS MEASURING 9X8X4CM.	INTACT	NA	NA	NA	RIGHT OVARIAN MASS	ABSENT	NA	9X8X4CM	SOLID. GREY WHITE HEMORRHAGIC	NA	NA
LEFT OVARY MEASURES 9X7X3.4CM.LEFT FT MESURES 2.5CM.	NA	INTACT	NA	INTACT	LEFT OVARY	ABSENT	ABSENT	9X7.5X3.4CM	SOLID AND CYSTIC.MUCOID AREAS NOTED. NO PAPILLARY EXCRESCENCES NOTED.	ABSENT	ABSENT
MEASURE 4.5X4X3.2CM	INTACT	NA		NA	RIGHT OVARIAN MASS	ABSENT	ABSENT	3X3X3CM	SOLID CYSTIC	ABSENT	NA
RIGHT OVARY MEASURES 5X4X3CM. LEFT OVARY MEASURES 4X4X3CM. LEFT	INTACT	INTACT	NA	INTACT	B/L OVARIES AND LEFT FT	ABSENT	ABSENT	RIGHT OVARY-5X4X3CM. LEFT OVARY-4X4X3CM	SOLID	ABSENT	ABSENT
RIGHT OVARY MEASURES-12X6X5CM. LEFT OVARY MEASURES 15X12X6CM.LEFT FT MEASURES 6 CM		INTACT	INTACT	NA	RIGHT AND LEFT OVARY	ABSENT	ABSENT	RIGHT OVARY-6X5X4CM.LEFT OVARY-1X1X0.5CM.	SOLID AND CYSTIC .SEROMUCINOUS FLUID DRAINED OUT.	NA	NA
MEASURES 1 CM IN LENGTH	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
MEASURES 4X4X4CM	INTACT	NA	INTACT	NA	RIGHT OVARY	ABSENT	ABSENT	4X3X2CM	SOLID CYSTIC	ABSENT	NA
RECEIVED A TRUCUT BX MEASURING 1 AND 1.2 CM IN LENGTH	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
MEASURES 5X4X3CM	INTACT	NA	INTACT	NA	RIGHT OVARY	ABSENT	ABSENT	4X4X3CM	SOLID	ABSENT	NA
BX MEASURE 1.3CM	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
RIGHT OVARAY 5X5X3CM LEFT OVARY 5X4X3CM	INTACT	INTACT	INTACT	INTACT	BL OVARIES	ABSENT	ABSENT	RIGHT 4X4X2CM LEFT 4X3X3CM	SOLID	ABSENT	NA
RECEIVED MULTIPLE TRUCUT BX STRIPS RANGING FROM 0.1 TO 0.2 CM.	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
RECEIVED AN OVARIAN MASS MEASURING 6X4X3CM.	INTACT	NA	NA	NA	NA	ABSENT	NA	6X4X3CM	SOLID	NA	NA
RECEIVED MULTIPLE NODULAR OVARIAN MASS ATTACHED TO A FT AND SEPARATELY LYING OMENTUM	INTACT	NA	INTACT	NA	RIGHT OVARIAN MASS	ABSENT	ABSENT	17X12X7CM	GREY WHITE NECROTIC	NA	RH
RIGHT OVARIAN MASS MEASURES 18X14X10CM.	INTACT	NA	NA	NA	RIGHT OVARY	ABSENT	NA	18X14X10CM	SOLID AND GREY WHITE	NA	NA
RIGHT ADNEXAL MASS MEASURING 10X8X6 CM	INTACT	NA	NA	NA	RIGHT OVARY	ABSENT	NA	10X8X6CM	SOLID	NA	NA
RIGHT OVARIAN MASS MEASURED 20X12X10CM.	INTACT	NA	NA	NA	RIGHT OVARY	ABSENT	NA	20X12X10CM	SOLID CYSTIC .STRAW COLOURED FLUID DRAINED OUT. PAPILLARY EXCRESENCES NOTED	NA	NA
TRUCUT BX MEASURING 0.8CM LEFT OVARY MEASURES 4X4X3CM	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

LARGE AREAS OF NECROSIS WITH PRESENCE OF CELLULAR TM WITH HIGH N:C RATIO IREGULAR NUCLEAR CONTOURS AND MOD CYTOPLASM. BIZARRE FORMS NOTED. BRISK	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	P(DIFFUSE)	ND	P	N	ND	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
PRESENCE OF CELLULAR TM WITH MOD NP HIGH N:C RATIO IREGULAR NUCLEAR CONTOURS AND MOD CYTOPLASM. BIZARRE FORMS NOTED WITH ATYPICAL MF	NG	HIGH GRADE	PAPILLARY ADENOCARCINOMA	P(DIFFUSE)	ND	P	N	ND	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
TM ARRANGED IN NESTS VN PN AND MOD CYTOPLASM. PSAMMOMA BODIES NOTED.	NG	HIGH GRADE	PAPILLARY ADENOCARCINOMA	P(DIFFUSE)	ND	P	N	ND	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
LARGE AREAS OF NECROSIS WITH VIABLE AREAS SHOWING CELLULAR TM ARRANGED IN DIFFUSE SHEETS. IX TM CELLS SHOW MOD NP, VN, PN AND MOD CYTOPLASM	NG	HIGH GRADE	PAPILLARY ADENOCARCINOMA	P(DIFFUSE)	ND	P	N	ND	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	N	P(DIFFUSE)	ND	ND
NCELLULAR TM ARRANGED IN PAPILLAE CRIBRIFORM SOLID AND OCCASIONAL GLANDS. IX TM CELLS EXHIBIT MOD NP VN PN MOD CYTOPLASM. AREAS OF NECROSIS AND BRISK	NG	HIGH GRADE	ADENOCARCINOMA	P(DIFFUSE)	ND	ND	ND	ND	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
TUMOUR CELLS ARRANGED IN PAPILLAE HAVING VN PN AND MODERATE CYTOPLASM. LARGE AREAS OF NECROSIS SEEN	NG	HIGH GRADE	ADENOCARCINOMA	N	ND	ND	ND	ND	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
WELL CIRCUMSCRIBED CELLULAR TM INTERSECTING FASCICLES AND STORIFORM PATTERN. IX TM CELLS BLAND SPINDLE OVOID NUCLEI SCANTY CYTOPLASM. AREAS OF HGH NECROSIS SEEN.	NG	NA	SPINDLE CELL NEOPLASM POSSIBLY SEX CORD STROMAL TUMOUR	ND	ND	ND	ND	ND	ND	ND	ND	ND	N	ND	P	ND	ND	ND	P(FOCAL)
ENCAPSULATED CELLULAR TM SPINDLE TO OVAL CELLS WITH BLAND NUCLEI SCANTY CYTOPLASM WITHIN COLLAGENISED STROMS.AREAS OF HGH NECROSIS SEEN. CYSTIC CHANGE NOTED. NO CAPSULAR BREECH NUCLEAR ATYPIA MITOSIS SEEN . RETICULIN	NG	NA	SPINDLE CELL NEOPLASM POSSIBLY SEX CORD STROMAL TUMOUR	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(FOCAL)	ND	ND	ND	ND	ND	N
WELL CIRCUMSCRIBED CELLULAR TM INTERSECTING FASCICLES AND STORIFORM PATTERN. IX TM CELLS BLAND SPINDLE OVOID NUCLEI SCANTY CYTOPLASM. AREAS OF HGH NECROSIS SEEN.	NG	NA	SPINDLE CELL NEOPLASM POSSIBLY SEX CORD STROMAL TUMOUR	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(FOCAL)	ND	ND	ND	ND	ND	N
CYSTS WHICH ARE PRIMARILY LINED BY TALL COLUMNAR MUCIN SECRETING EPITHELIUM. THERE IS LINING OF CILIATED CUBOIDAL EPITHELIUM HAVING EOSINOPHILIC CYTOPLASM. HSLM SEEN.AREAS OF PAPILLARY TUFTING NUCLEAR STRATIFICATION SEEN. NO STROMAL /CAPSULAR INVASION SEEN	NG	NA	ADENOCARCINOMA WITH SEROMUCINOUS DIFFERENTIATION	P	P	P	P(FOCA	ND	ND	ND	N	ND	N	ND	P	ND	ND	ND	ND
TM IN GLANDS IX CELLS VN AND MOD CYTOPLASM	NG	NA	LOW GRADE SEROUS CARCINOMA	P	P	ND	N	ND	ND	ND	ND	ND	N	ND	P	ND	WILD TYPE	ND	ND
TM IN SHEETS & GLANDS IX CELLS VN PN AND MOD CYTOPLASM	NG	NA	HIGH GRADE ADENOCARCINOMA POSSIBLY ENDOMETRIOID CARCINOMA RESEMBLING SEX CORD	P	N	P	N	N	ND	ND	ND	ND	N	ND	P	ND	ND	ND	N
CELLULAR TM IN GLANDS WITH BACK TO BACK ARRANGEMENT. IX TM CELLS MOD NP VN ICN MOD CYTOPLASM.	NG	NA	ADENOCARNOMA POSSIBLY ENDOMETRIOID CARCINOMA	P	P	P	ND	P	ND	ND	ND	ND	N	ND	P	ND	WILD TYPE	ND	ND
CELLULAR TM IN TUBULOVILLOUS PATTERN GLANDS SOLID NESTS MOD NP VN PN MOD CYSTOPLASM	NG	NA	ADENOCARNOMA POSSIBLY ENDOMETRIOID CARCINOMA	P	P	ND	ND	P	ND	ND	ND	ND	N	ND	P	ND	P(WILD)	ND	ND
TM IN GLANDS IX CELLS VN AND MOD CYTOPLASM	NG	NA	ADENOCARNOMA POSSIBLY ENDOMETRIOID CARCINOMA	P	N	N	ND	P	ND	ND	ND	ND	N	ND	P	N	P(WILD)	ND	ND
CELLULAR TM IN GLANDS CYSTS PAPILLAE. IX TM CELLS MOD NP VN PN SCANT CYTOPLASM. AREAS IN NECROSIS AND DC SEEN NO CAPSULAR BREECH	NG	NA	ADENOCARNOMA POSSIBLY ENDOMETRIOID CARCINOMA	P	P	N	N	P	ND	ND	ND	ND	N	ND	P	ND	ND	ND	ND
CELLULAR TM IN GLANDS WITH BACK TO BACK ARRANGEMENT. IX TM CELLS MOD NP VN ICN MOD CYTOPLASM.	NG	NA	ADENOCARNOMA POSSIBLY ENDOMETRIOID CARCINOMA	P	P	N	ND	P	ND	ND	ND	ND	N	ND	P	ND	P (WILD)	ND	ND
SOILD NESTS GLANDS IX TM CELLS VN PN MOD CYSTOPLASM LARGE AREAS OF NECROSIS SQUAMOUS MORULES SEEN	NG	NA	ADENOCARNOMA POSSIBLY ENDOMETRIOID CARCINOMA	P	P	N	ND	P	ND	ND	ND	ND	N	ND	P	ND	WILD TYPE	ND	ND
TM IN GLANDS IX CELLS VN AND MOD CYTOPLASM	NG	NA	ADENOCARNOMA POSSIBLY ENDOMETRIOID CARCINOMA	P	P	ND	ND	P	ND	ND	ND	ND	N	ND	P	ND	ND	ND	ND
TM IN GLANDS IX CELLS VN AND MOD CYTOPLASM	NG	NA	ADENOCARNOMA POSSIBLY ENDOMETRIOID CARCINOMA	P	P	P	N	P	ND	ND	ND	ND	N	ND	P	ND	ND	N	ND
CELLULAR TM SEPARATED BY FIBROUS SEPTAE INFILTRATED BY LYMPHOCYTES. TM CELLS LARGE MULTIFORM POLYGONAL CELLS VN PN MOD CYTOPLASM. FOCI OF HGH AND NECROSIS SEEN TM REACHING UPTO CAPSULE	NG	NG	GERM CELL TUMOUR POSSIBLR DYSGERMINOMA	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
CELLULAR TM IN NESTS SEPARATED BY FIBROUS SEPTA INFILTRATED BY LYMPHOCYTES. POLYGONAL CELLS VN PN MOD CYTOPLASMHGH OCC MF TM REACHING UPTO CAPSULE	NG	NG	GERM CELL TUMOUR POSSIBLR DYSGERMINOMA	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
CELLULAR TM IN NESTS SEPARATED BY FIBROUS SEPTA INFILTRATED BY LYMPHOCYTES. POLYGONAL CELLS VN PN MOD CYTOPLASMHGH OCC MF TM IS INVADING CAPSULE	NG	NG	GERM CELL TUMOUR POSSIBLR DYSGERMINOMA/ EMBRYONAL CARCINOMA	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
CELLULAR TM ARRANGED IN TUBULOCYSTIC, PAPILLARY AND SOLID PATTERN. IX TM CELLS MOD PLEOMORPHIC ROUND TO ANGULATED VN PN MOD AMT OF CLEAR TO EOSINOPHILIC CYTOPLASM WITH HOBNAILING AT PLACES. STROMAL HYALINISATION AND HYALINE GLOBULES NOTED. AREAS OF NECROSIS SEEN. NO LVU/CAPSULAR BREECH NOTED	NG	NG	MALIGNANT NEOPLASM	N	ND	ND	ND	P	ND	ND	ND	ND	N	ND	ND	ND	ND	P	ND
CELLULAR TM PAPILLARY CONFIGURATION PAPILLAE LINED BY LARGE CELLS ROUND VN PN MOD CYTOPLASM. SURROUDING THESE CELLS HAVE SPINDLE NUCLEI VESICULAR CHROMATIN ILL DEFINED CYTOPLASM. FOCUS OF CARTILAGE SEEN.	NG	NG	NA	ND	ND	P(EPIT	ND	P(EPITH	ND	ND	ND	ND	P(EPITHELIAL	ND	P(SPINDLE CE	ND	ND	ND	ND

ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	70%	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
N	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	10%	ND	ND	SMA POSITIVE DESMIN NEGATIVE S100 NEGATIVE	FIBROMA	FIBROMA
N	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	SMA POSITIVE DESMIN NEGATIVE	FIBROMA	FIBROMA
N	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	SMA POSITIVE DESMIN NEGATIVE	FIBROMA	FIBROMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	N	ND	ENDOMETRIOID CARCINOMA WITH SEROMUCINOUS DIFFERENTIATION	ENDOMETRIOID CARCINOMA WITH SEROMUCINOUS DIFFERENTIATION
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	N	ND	ND	ND	ND	ND	ND	ENDOMETRIOID CARCINOMA	ENDOMETRIOID CARCINOMA
N	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ENDOMETRIOID CARCINOMA RESEMBLING SEX CORD	ENDOMETRIOID CARCINOMA RESEMBLING SEX CORD
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(FOCA	ND	ND	ND	ND	ND	ND	ENDOMETRIOID CARCINOMA	ENDOMETRIOID CARCINOMA FIGO
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ENDOMETRIOID CARCINOMA	ENDOMETRIOID CARCINOMA FIGO
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(FOCA	ND	ND	ND	ND	ND	ND	ENDOMETRIOID CARCINOMA	ENDOMETRIOID CARCINOMA FIGO
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ENDOMETRIOID CARCINOMA	ENDOMETRIOID CARCINOMA FIGO
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ENDOMETRIOID CARCINOMA	ENDOMETRIOID CARCINOMA FIGO GRADE 2
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ENDOMETRIOID CARCINOMA	ENDOMETRIOID CARCINOMA FIGO
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(FOCA	ND	ND	ND	N	ND	ND	ENDOMETRIOID CARCINOMA	ENDOMETRIOID CARCINOMA FIGO
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ENDOMETRIOID CARCINOMA	ENDOMETRIOID CARCINOMA FIGO
ND	ND	ND	P	P	ND	ND	ND	ND	ND	ND	ND	ND	N	ND	ND	ND	ND	ND	ND	OCT4 POSITIVE	DYSGERMINOMA	DYSGERMINOMA
ND	ND	ND	P	P	N	ND	ND	P	ND	ND	ND	ND	N	ND	ND	ND	ND	ND	ND	OCT4 POSITIVE CK NEGATIVE	DYSGERMINOMA	DYSGERMINOMA
ND	ND	ND	P	P	ND	ND	ND	P	ND	N	ND	ND	N	ND	ND	ND	ND	ND	ND	PAN CK NEGATIVE OCT 4 POSITIVE	DYSGERMINOMA	DYSGERMINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(DIFF	ND	ND	ND	ND	ND	ND	CLEAR CELL CARCINOMA FIGO GRADE 1A	CLEAR CELL CARCINOMA FIGO GRADE 1A
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	OCT4 NEGATIVE	CARCINOSARCOMA	CARCINOSARCOMA

74	S	58F	1119545	21-4548	739/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TAH BSO
75	RG	72F	1215777	21-11326	1268/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	RIGHT ADENEXAL MASS
76	SV	21F	971437	20-6746	795/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	429	NA	NA	233	NA	ND	RIGHT OVARY WITH RIGHT FT
77	HK	74F	955694	20-7620	926/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	30.9	6	NA	NA	NA	ND	LEFT OVARIAN MASS AND TAH WITH BSO OMENTUM LEFT AND RIGHT
78	S	28F	973314	20-6889	823/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	LEFT OVARY AND FT
79	BK	36F	934117	20-4546	439/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	12.7	NA	NA	NA	NA	ND	OUTSIDE BLOCKS
80	S	27F	956338	20-6020	679/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	RIGHT OVARIAN MASS RIGHT LN RIGHT PERITONEUM OMENTAL BX
81	PK	48F	976479	20-7151	874/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	9.6	NA	NA	NA	NA	ND	TAH WITH BSO OMENTUM LEFT AND B/L PERITONEUM
82	JK	43F	965282	20-6424	755/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	TAH BSO B/L FT WITH RIGHT CYSTIC OVARY
83	GK	45F	1157376	21-7558	928/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	20.7	0.2	NA	NA	NA	ND	LEFT ADENEXAL MASS
84	JK	65F	1226941	22-148	81/22	PATIENT IS A KCO CARCINOMA ENDOMETRIUM	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	13.8	NA	NA	NA	NA	ND	TAH BSO LEFT RIGHT PELVIC LN
85	SK	49 F	978993	20-7329	878/2020	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	32.8	NA	NA	NA	NA	ND	TOTAL HYSTERECTOMY AND BILATERAL SALPINGO-OOPORECTOMY, RIGHT AND LEFT PELVIC LNS AND PERITONEAL BIOPSY
86	AK	17F	942756	20-6670	781/20	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	1.13	174	NA	ND	RIGHT AND LEFT OVARY
87	SK	47F	203774	21-6477	779/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	785	NA	18.53	NA	NA	ND	TRUCUT BX LEFT ADENEXA
88	SK	60F	1021234	21-974	156/21	NA	0	NEG	NEG	NEG	WNL	WNL	WNL	WNL	NA	NA	NA	NA	NA	ND	OVARY

RIGHT OVARY MEASURES 5X4X1CM.	INTACT	NA	NA	NA	RIGHT OVARY	ABSENT	ABSENT	5X4X1CM.	SOLID AND GREY WHITE	NA	NA
RECEIVED AN ALREADY CUT OPEN CYSTIC STRUCTURE MEASURING	INTACT	NA	NA	NA	RIGHT OVARY	ABSENT	NA	4X3X2CM	SEROUS FLUID DRAINED OUT. SOLID AND CYSTIC	NA	NA
RECEIVED MULTIPLE NODULAR GREY WHITE SOFT TISSUE PIECES TOGETHER	INTACT	NA	INTACT	NA	RIGHT OVARY	ABSENT	ABSENT	8X6X5.5CM	SOLID, CYSTIC AND HEMORRHAGIC	NA	NA
OVARIAN MASS MEASURED 20x18x10cm	INTACT	INTACT	INTACT	INTACT	LEFT OVARY	ABSENT	ABSENT	12X8X6CM	SOLID AND CYSTIC	ABSENT	RH
RECEVIED MULTIPLE GREY WHITE	NA	INTACT	NA	INTACT	LEFT OVARY	ABSENT	ABSENT	8X6X1CM	SOLID	NA	NA
TECHNICALLY POOR PREPARATION	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
RECEIVED A WELL ENCAPSULATED TUBOOVARIAN MASS WITH PART OF	INTACT	INTACT	NA	NA	RIGHT OVARIAN MASS	ABSENT	ABSENT	6X5X3.5CM	SOLID AND CYSTIC	ABSENT	RH
RIGHT OVARIAN MASS MEASURES 8X6X3CM. FT MEASURES 5 CM.	INTACT	INTACT	INTACT	INTACT	RIGHT OVARY	ABSENT	ABSENT	6X4X3CM	SOLID AND CYSTIC. PAPILLARY EXCRESENCES NOTED.	ABSENT	RH
RIGHT ADENEXA- CYSTIC MASS MEASURES 10X4.5X2CM.	INTACT	NA	INTACT	INTACT	RIGHT OVARY	ABSENT	ABSENT	5X3X1CM.	SOLID AND CYSTIC	NA	NA
LEFT ADNEXAL MASS MEASURING 6X4X3.9CM	NA	INTACT	NA	NA	LEFT ADNEXA	ABSENT	NA	6X4X3CM	SOLID	NA	NA
RIGHT OVARY MEASURES 5X5X4 CM	INTACT	INTACT	NA	NA	B/L OVARIES	NA	NA	5X5X3 CM 4X4X2 CM	SOLID CYSTIC .	NA	NA
LEFT AND RIGHT OVARY	PAPILLARY EXCRESCENCES ON CAPSULE	PAPILLARY EXCRESCENCES ON CAPSULE	NA	NA	RIGHT OVARY LEFT OVARY	PRESENT- RIG	NA	RIGHT OVARY-12X10X5 cm LEFT OVARY- 12X9X8cm	CYSTIC AND SOLID. MUCOID MATERIAL DRAINED OUT.	ABSENT	UNIVOLVED
RIGHT OVARIAN MASS MAESURES 12X11X4.5CM. RIGHT FT MEASRES 6CM. LEFT OVARIAN MASS MEASURES	INTACT	INTACT	INTACT	INTACT	RIGHT AND LEFT OVARY	B/L OVARIAN	ABSENT	RIGHT OVARY-12X11X4.5CM LEFT OVARY- 5.5X5X2CM	RIGHT OVARY-GREYWHITE NECROTIC LEFT OVARY- SOLID AND CYSTIC	NA	NA
TRUCUT BX MEASURING 1CM IN LENGTH	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
RECEIVED A TRUCUT BX MEASURING 1 CM IN LENGTH	NA	NA	NA	NA	OVARY	NA	NA	NA	NA	NA	NA

WELL CIRCUMSCRIBED TM HAVING OVAL IRREGULAR NESTS SURROUNDED BY ABUNDANT FIBROMATOUS STROMA. NESTS OF TRANSITIONAL CELLS BLAND OVAL	NG	NA	NEOPLASM POSSIBLY BRENNERS TUMOUR	ND	ND	P	ND	ND	ND	P(FOC	P	ND	ND	ND	P	N	ND	ND	ND
WELL CIRCUMSCRIBED TM HAVING OVAL IRREGULAR NESTS SURROUNDED BY ABUNDANT FIBROMATOUS STROMA. NESTS OF TRANSITIONAL CELLS BLAND OVAL	NG	NA	NG	ND	ND	P	N	ND	ND	ND	ND	ND	ND	ND	ND	P	ND	ND	ND
CELLULAR T IN NESTS SHEETS OCCASIONAL SURVIVAL PATTERN.IX TM CELLS VN MOD CYTOPLASM. NUCLEAR GROOVES PRESENT. EXTENSIVE NECROSIS EXTRACELLULAR	NG	NG	SEX CORD STROMAL TUMOUR	P	ND	N	ND	N	ND	N	ND	ND	P(WEAK)	ND	P	ND	ND	ND	P(FOCAL)
CELLULAR TM WITH CELLS ARRANGED IN NESTS SHEETS MICROFOLLICULAR PATTERN ARRANGED AROUND BLOOD VESSELS FOCALLY. TM CELLS HAVE VESICULAR ELONGATED	NG	NG	SEX CORD STROMAL TUMOUR POSSIBLY GRANULOSA CELL	P (WEAK)	ND	N	ND	ND	ND	N	ND	ND	P	ND	ND	ND	ND	ND	P(FOCAL)
CELLULAR TM WITH CELLS ARRANGED IN SHEETS NESTS AND ISLANDS. TM CELLS HAVE	NG	NG	SEX CORD STROMAL TUMOUR	ND	ND	N	ND	ND	ND	ND	ND	ND	N	ND	ND	ND	ND	ND	P(FOCAL)
CELLULAR TM WITH CELLS ARRANGED IN SHEETS NESTS AND ISLANDS. TM CELLS HAVE	NG	NG	SEX CORD STROMAL TUMOUR	ND	ND	ND	ND	ND	ND	ND	ND	ND	N	ND	ND	ND	ND	ND	P(FOCAL)
CELLULAR TM ARRANGED IN SHEETS AND NESTS. TM CELLS ARE SPINDLE TO OVAL WITH VN CN AND MODERATE CYTOPLASM. BRISK MITOSIS NOTED. NO LVI SEEN.	NG	NG	SEX CORD STROMAL TUMOUR POSSIBLY GRANULOSA CELL	ND	ND	N	ND	ND	ND	N	ND	ND	N	ND	ND	ND	ND	ND	P(FOCAL)
CELLULAR TM ARRANGED IN SHEETS, NESTS, MICROFOLLICLES, MACROFOLLICLES AND FEW CYSTIC SPACES FILLED WITH EOSINOPHILIC MATERIAL. TM CELLS HAVE VN PN AND MODERATE CYTOPLASM. FEW CELLS HAVE NUCLEAR GROOVESFOCI OG HGH AND OCCASIONAL MF SEEN.	NG	NG	SEX CORD STROMAL TUMOUR POSSIBLY GRANULOSA CELL TUMOUR	ND	ND	N	ND	ND	ND	ND	ND	ND	N	ND	ND	ND	ND	ND	P(FOCAL)
CELLULAR TM IN DIFFUSE SHEETS FOCAL CORDS TRABECULAE. IX TM CELLS HAVE ROUND TO OVAL NUCLEI SCANT CYTOPLASM. NUCLEAR GROOVES SEEN.NO CAPSULAR INVASION.	NG	NG	SEX CORD STROMAL TUMOUR POSSIBLY GRANULOSA CELL TUMOUR	ND	ND	ND	ND	ND	ND	N	ND	ND	P	ND	ND	ND	ND	ND	P(FOCAL)
CELLULAR TM ARRANGED IN SOLID SHEETS TRABECULAE MACROFOLLICLES. IX TM CELLS ROUND TO OVAL NUCLEI PN MOD TO ABUNDANT EOSINOPHILIC CYTOPLASM NUCLEAR GROOVES SEEN IN SOME. CYSTIC CHANGE NOTED. NO CALL EXNER BODIES SEEN CAPSULAR INVASION NUCLEAR ATYPIA MF SEEN	NG	NG	SUGGESTIVE OF GRANULOSA CELL TUMOUR	ND	ND	ND	ND	ND	ND	N	ND	ND	N	ND	ND	ND	ND	ND	P(FOCAL)
CELLULAR TM IN TRABECULAE CORDS SOLID PATTERN FOLLICLE IX TM CELLS VN NUCLEAR GROOVES NO CAPSULAR INVASION	NG	NG	SUGGESTIVE OF GRANULOSA CELL TUMOUR	ND	ND	ND	ND	ND	ND	ND	ND	ND	P	ND	ND	N	ND	ND	P(FOCAL)
BILATERAL OVARIES SHOW A CYSTIC TUMOR WITH PRESENCE OF HIERARCHIAL BRANCHING PAPILLAE .PAPILLARY CORES EXHIBIT DENSE FIBROUS STROMA AND ARE LINED BY CELLS HAVING VN,PN AND MODERATE AMOUNT OF CYTOPLASM.NUCLEAR STRATIFICATION NOTED.FOCAL TUMOR CELLS INFILTRATION INTO UNDERLYING	NG	LOW GRADE		P	ND	ND	ND	ND	ND	ND	ND	ND	P	ND	ND	ND	P(FOCAL)	ND	ND
CELLULAR TM RETICULAR PATTERN TRABECULAE NETS PAPILLAE PSEUDOGLANDS POLYVESICULAR PATTERN.TM CELLS VN PN MOD CYTOPLASM NO GIANT CELLS SEEN	NG	NG	GERM CELL TUMOUR POSSIBLY YOLK SAC TUMOUR	P	ND	DOT L	ND	N	ND	ND	ND	ND	P(WEAK)	ND	ND	ND	ND	ND	N
EXTENSIVE AREAS OF NECROSIS WITH VIABLE AREAS SHOWING CELLULAR TM ARRANGED IN NESTS AND SHEETS. IX TM CELLS SHOW MOD NP, VN, PN AND MOD CYTOPLASM. ATYPICAL MF SEEN.	NG	HIGH GRADE	CARCINOMA POSSIBLY HIGH GRADE SEROUS CARCINOMA	P (DIFFUSE)	ND	ND	ND	P	ND	ND	ND	ND	P(DIFFUSE)	ND	ND	ND	P(DIFFUSE)	ND	ND
TM IN GLANDS IX CELLS VN AND MOD CYTOPLASM	NG	NA	HIGH GRADE ADENOCARCINOMA POSSIBLY ENDOMETRIOID CARCINOMA	P	P	ND	ND	ND	ND	ND	ND	ND	N	ND	P	ND	ND	N	ND

ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P63 POSITIVE	BRENNERS TUMOUR	BRENNERS TUMOUR
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P63 POSITIVE	BRENNERS TUMOUR	BRENNERS TUMOUR
P	ND	ND	N	N	N	N	ND	ND	N	N	ND	ND	N	ND	ND	ND	ND	ND	N	LCA- N S100- N HEPPAR 1- N	ANAPLASTIC VARIANT OF JUVENILE	ANAPLASTIC VARIANT OF JUVENILE GRANULOSA
P(FOCAL)	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ADULT GRANULOSA CELL TUMOUR	ADULT GRANULOSA CELL TUMOUR
P(FOCAL)	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ADULT GRANULOSA	ADULT GRANULOSA CELL
P(FOCAL)	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ADULT GRANULOSA	ADULT GRANULOSA CELL
P(FOCAL)	ND	ND	ND	ND	ND	ND	ND	ND	N	N	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ADULT GRANULOSA CELL TUMOUR	ADULT GRANULOSA CELL TUMOUR
P(FOCAL)	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ADULT GRANULOSA CELL TUMOUR	ADULT GRANULOSA CELL TUMOUR
P(FOCAL)	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ADULT GRANULOSA CELL TUMOUR	ADULT GRANULOSA CELL TUMOUR
P(DIFFUSE)	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ADULT GRANULOSA CELL TUMOUR	ADULT GRANULOSA CELL TUMOUR
P(FOCAL)	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ADULT GRANULOSA CELL TUMOUR	ADULT GRANULOSA CELL TUMOUR
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	P(PATC	ND	ND	ND	ND	ND	ND	SEROUS BORDERLINE TUMOUR	SEROUS BORDERLINE TUMOUR
P	ND	ND	N	N	N	N	ND	ND	N	N	ND	ND	N	ND	ND	ND	10%	ND	N	ND	JUVENILE GRANULOSA CELL TUMOUR	JUVENILE GRANULOSA CELL TUMOUR
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	HIGH GRADE SEROUS CARCINOMA	HIGH GRADE SEROUS CARCINOMA
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	CK POSITIVE OCT 4 POSITIVE	ENDOMETRIOID CARCINOMA	ENDOMETRIOID CARCINOMA FIGO GRADE 1

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Date 6/1/2022

The Principal,
DMC, Ludhiana.

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 29.10.2021 has approved the plan of thesis of **Mehar Ghuman**, a student of your college for **MD Pathology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
Immunohistochemical spectrum of ovarian neoplasms.

Supervisor
Dr. Harpreet Kaur
Prof. & Head,
Dept. of Pathology,
DMCH, Ludhiana.

Co-Supervisor

Dr. Aminder Singh
Assoc. Prof.,
Dept. of Pathology,
DMCH, Ludhiana.

Dr. Kunal Jain
Asst. Prof.,
Dept. of Oncology,
DMCH, Ludhiana.

The student has to submit the four copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

95. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*
96. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

IMMUNOHISTOCHEMICAL SPECTRUM OF OVARIAN NEOPLASMS

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

IN

PATHOLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

MARCH, 2021

DR. MEHAR GHUMAN

DEPARTMENT OF PATHOLOGY

DAYANAND MEDICAL COLLEGE AND HOSPITAL

LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	IMMUNOHISTOCHEMICAL SPECTRUM OF OVARIAN NEOPLASMS
For the degree of	MD (PATHOLOGY)
Name of the candidate	Dr. Mehar Ghuman
Supervisor	Dr Harpreet Kaur, Professor & Head, Department of Pathology, DMCH, Ludhiana
Co-supervisor(s)	Dr Aminder Singh, Associate Professor, Department of Pathology, DMCH, Ludhiana Dr. Kunal Jain, Assistant Professor, Department of Oncology, DMCH,Ludhiana
Institution	Dayanand Medical College and Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: All the cases of ovarian neoplasms on which Immunohistochemistry (IHC) will be conducted will be analyzed.

Aims & Objectives: To study the immunohistochemical spectrum of ovarian neoplasms.

Material & Methods: This 2 year study, of which 1 year (1_{st} March 2020- 28_{th} February 2021) is retrospective and 1 year (1_{st} March 2021- 28_{th} February 2022) is prospective, will be conducted in the Department of Pathology, Dayanand Medical College and Hospital, Ludhiana. All the histopathologically diagnosed ovarian neoplasms in which IHC studies will be done received in the Department of Pathology, Dayanand Medical College and Hospital, Ludhiana will be included in the study. Slides will be subjected to IHC examination under both low power(100x) and high power(400x).

Clinical Significance: To obtain a good database for accuracy of the diagnosis of immunohistochemistry and its correlation with the histopathological findings in ovarian neoplasms.

Keywords: Neoplasms, Ovary, Epithelial, Sex Cord, Immunohistochemistry(IHC).

(Signature)	(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"IMMUNOHISTOCHEMICAL SPECTRUM OF OVARIAN NEOPLASMS"** exist in the Department of Pathology, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate herself under our supervision and guidance.

Supervisor

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Professor & Head
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Co Supervisors

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Head of the Department

Dr. Harpreet Kaur
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Place : _____

Date : _____

APPROVAL PROFORMA
BY RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Mehar Ghuman
Department	Pathology
Topic of Thesis	IMMUNOHISTOCHEMICAL SPECTRUM OF OVARIAN NEOPLASMS
Likely date of appearing in PG examination	May 2023
Date of enrollment	26th July, 2020
Name of Head of Department	Dr. Harpreet Kaur
1) Supervisor **2) Co-Supervisor(s)**	Dr. Harpreet Kaur Dr. Aminder Singh Dr. Kunal Jain
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
Dr. Jaspal Singh (Professor & Head, Surgery)	Dr. Ramit Mahajan (Associate Professor, Gastroenterology)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)	Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)
Dr. Gurpreet S Wander (Vice Principal)	Dr. Gurpreet S Wander (Vice Principal & Professor & Head, Cardiology)
	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / No

Dr. Sandeep Puri
Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	Dr. Mehar Ghuman 90-A, Sarabha Nagar,Ludhiana
2	NAME OF THE INSTITUTE	Dayanand Medical College and Hospital, Ludhiana
3	COURSE OF STUDY AND SUBJECT	MD Pathology
4	DATE OF ADMISSION OF COURSE	26-07-2020
5	TITLE OF THE TOPIC	IMMUNOHISTOCHEMICAL SPECTRUM OF OVARIAN NEOPLASMS

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Ovarian cancer is the sixth most common cancer and the seventh leading cause of cancer deaths among women worldwide. In most of the population-based cancer registries in India, ovarian cancer is the third leading cancer among women, trailing behind cervix and breast cancer.[1] Ovarian cancer has the worst prognosis among all gynecological malignancies. The overall 5-year survival is approximately 45%, primarily due to the late stage at diagnosis of the disease.[2]

Ovarian tumors are characterized by huge heterogeneity in their clinical presentation, so an accurate histopathological diagnosis is required. World Health Organization (WHO) classifies ovarian tumors as per their most probable cell of origin and histomorphological features.[3] Immunohistochemistry is helpful in a large number of cases where the morphology and clinical features alone do not allow definite diagnosis of tumor present in tissue sections.[4]

More than 90% of ovarian tumours are “epithelial” in origin. Surface epithelial tumors are further classified by cell type (serous, mucinous, endometrioid, etc) and atypia (benign, borderline [atypical proliferation, low malignant potential] or (malignant; malignant may be invasive or non-invasive).Most malignant tumors are surface epithelial (90%) type. Sometimes the fallopian tube epithelial lining is the precursor lesion of some ovarian tumours.[5] Ovarian neoplasms are characterized by changes in their receptor status and consequently, tumor can be either primary receptor negative or as a result of their progression, they may lose the receptors.[6] Ki-67 is a proliferation marker helpful in predicting disease outcome in many types of malignancies including ovarian neoplasms.[7] Studies have shown that the p53 gene is mutated in 30-80% of ovarian carcinomas.[8] IHC is now used not only for diagnosis but also for other parameters including prognosis, microscopic tumor staging, prediction of response to therapy and for the selection of therapeutic agents and analysis of the IHC profile of ER, PR, Ki-67 and

p53 in various ovarian epithelial tumours, CD117, PLAP, AFP etc in various germ cell tumours, FOXL2, SF-1, inhibin in various sex cord tumours. Markers of neuroendocrine differentiation are helpful in the diagnosis of primary and metastatic neuroendocrine carcinomas and primitive neuroectodermal tumours (PNETS) and for identification of primary and secondary carcinoid tumours. Chromogranin and synaptophysin are the most specific markers of neuroendocrine differentiation in general use. NSE and CD56 (neural cell adhesion molecule; NCAM) are less specific but are more sensitive and should be used for screening purposes only.

Immunohistochemistry (IHC) has become a gold standard method of diagnosis for surgical pathology. Because of the diversity of diagnoses and often subtle nature of diagnostic criteria, IHC finds particular utility in ovarian tumours. The use of progressively small amounts of tissue for diagnosis highlights the importance of this method. The sensitivity and crispness of IHC stains have progressively improved with the advent of new techniques. The immunohistochemistry technique is used in the search for cell or tissue antigens ranging from amino acids and proteins to infectious agents and specific cellular populations. The technique comprises of two steps:

A: slide preparation (specimen fixation and tissue processing) and stages evolved for the reaction (in order as given: antigen retrieval, non-specific site block endogenous peroxidase block, primary antibody incubation, and the employment of systems of detection, revealing and counterstaining and also slide mounting and storage).

B: interpretation and quantification of the obtained expression.[9]

6.2 REVIEW OF LITERATURE

The World Health Organization histological classification for ovarian tumors separates ovarian neoplasms according to the most probable tissue of origin: surface epithelial (65%), germ cell (15%), sex cord-stromal (10%), metastases (5%) and miscellaneous.

Most malignant tumours are surface epithelial type. The need to ascertain a correlation between the histomorphological features and IHC findings wherever possible is needed for a definitive diagnosis.

Immunohistochemistry (IHC) technique is widely used in diagnostics and research, and its applications continue to be extended because of its easy utility, reliability and versatility.

Some of the commonly used IHC markers for ovarian neoplasms are:

Epithelial Ovarian Neoplasm:

Cytokeratin profile:- Nearly all of the primary epithelial tumors of the ovary are CK7 positive so lack of staining for CK7 suggests the possibility of metastasis. Except for mucinous tumors of intestinal type, stains for CK20 are usually negative in primary epithelial tumors.

CEA:- In ovarian cancers, CEA is not often positive except for mucinous adenocarcinoma, which is typically CEA positive.

EMA:- Diffuse positive staining for EMA suggests an epithelial tumor, either primary or metastatic, mimicking a sex cord–stromal tumor. Sex cord–stromal tumors are almost always EMA negative.

CA 125:- Staining of the cell membranes with CA 125 is typically positive in serous carcinoma.[9]

WT1:- Expression is seen in serous carcinoma of the ovary, fallopian tube, and peritoneum but expression in serous carcinoma of the endometrium tends to be limited.

β-catenin:- Among the epithelial tumors, endometrioid neoplasms are most likely to show nuclear and cytoplasmic staining for β-catenin.

ER, PR, Vimentin:- Seromucinous tumors frequently exhibit positive nuclear staining for estrogen and progesterone receptors and show positive cytoplasmic staining for vimentin.

GATA 3:- It has emerged as a useful marker for Brenner tumors, as most show diffuse positive staining with this marker.

p53:- A strong positive nuclear staining for p53 is found in 30% to 50% of serous carcinomas. Low grade serous carcinoma, which appears to evolve via a different pathway than high-grade serous carcinoma, is significantly less likely than high-grade serous carcinoma to express p53.[9]

Pax-8:- It is extremely useful in confirming müllerian origin.

Napsin A:-It is highly expressed in clear cell carcinomas of the ovary.[10]

Sex Cord-Stromal Tumours:-

Inhibin:- It is a sensitive and relatively specific marker of sex cord–stromal tumors of the ovary. **Inhibin, calretinin, and SF-1, FOXL2:-** Together these markers can be used in an IHC panel for positive identification of sex cord–stromal tumors.

Germ Cell Tumours:-

PLAP:- Placental alkaline phosphatase (PLAP) is a marker for malignant GCTs, especially dysgerminoma and embryonal carcinoma (ECa).

AFP:- Alpha-fetoprotein (AFP) is an oncofetal glycoprotein expressed in yolk sac tumor and its variants, including hepatoid and endometrioid yolk sac tumor.

CD117:- CD117 does not stain embryonal carcinoma (ECa) and is thus a more specific marker of dysgerminoma than is PLAP.

Glypican-3:- It is highly expressed by yolk sac tumors.

hCG:- Primary ovarian tumors that contain syncytiotrophoblastic cells, including choriocarcinoma and some dysgerminomas and embryonal carcinomas(ECas), express hCG.

SALL4:- It is a highly sensitive marker for yolk sac tumor, dysgerminoma, embryonal carcinomas (ECa), choriocarcinoma, and teratoma.[9]

Liliac *et al* in 2013 conducted a study to evaluate the role of PAX8 and WT1 in different types of ovarian cancer (OC) with focus on (i) the completion of evidences of the Müllerian origin and (ii) the establishment of primary ovarian tumor status vs. metastasis. The study group consisted of 86 cases, with histopathological diagnosis

covering the main subtypes of ovarian. One case was not valuable due to technical difficulties. Inference was made that PAX8 expression was positive in 70 (81.39%) cases, the remaining 15 (17.44%) negative cases suggested a non-Müllerian origin. WT1 expression was positive in 61 (71%) cases, mainly expressed in serous carcinoma, regardless of their differentiation degree, and negative in 24 (27%) cases.[11]

Khan *et al* in 2014 described that most (85-95%) of the ovarian cancers were classified as "epithelial" and were believed to arise from the surface epithelium of the ovary, 5 to 8 percent from stromal cells, and 3 to 5 percent from germ cells.[12] Among the secondary/ metastatic ovarian tumours, common primary sites were breast, colon and stomach.[13] They studied 80 cases of ovarian tumours over a period of one and half years . Out of the 80 cases of ovarian tumours, benign ovarian lesions were more common (75%) than malignant lesions (25%). Serous cystadenoma was the commonest benign tumor (45%). Overall surface epithelial carcinomas were responsible for 70% of all malignant lesions among which serous cyst adenocarcinoma was most common (45%). 88.8% cases of serous carcinomas showed diffuse positivity for CK7, 60% showed positivity for CA125 and 100% were negative for CK20. 100% cases of mucinous carcinoma showed positivity for CK7, 66.66% showed positivity for CEA and 100% were negative for CA125. ER and PR showed nuclear positivity in both cases (100%) of endometrioid carcinoma. Dysgerminoma showed positivity for placental alkaline phosphatase (PLAP). Yolk sac tumor was positive for alpha-feto protein (AFP). Embryonal carcinoma was positive for CD30. Granulosa cell tumor was positive for Calretinin and Inhibin and negative for AFP.

Donna *et al* in a study published in 2015 did a comparative analysis of Rb1, P16 and ER as diagnostic, prognostic and potential targets for therapeutic agents in ovarian epithelial tumors and did immunohistochemical study of 130 ovarian carcinomas. This study was aimed to determine the frequency of expression of Rb1, P16 and ER in ovarian epithelial tumors by immunohistochemistry. Conclusion was made that coordinate pattern of Rb1+ and ER+ in HGSC and LGSC

was 19 and 50 %, respectively. Rb1 and P16 showed inverse expression pattern according to tumor grade with more frequent Rb1 in low grade vs. more frequent P16 in grade 3 tumors.[14]

Naik *et al* in 2015 conducted a in which 110 cases were studied aged between 14-75 years. The study was undertaken to analyze the immunohistochemical (IHC) profile of estrogen receptors (ER), progesterone receptors (PR), Ki-67, and p53 in various ovarian epithelial tumors and attempted correlation with clinical and histopathological findings. Results stated that the expression of ER was more in malignant tumors than borderline and benign. As compared to ER, the expression of PR was more in benign than borderline and malignant tumors. The expression of p53 was less in benign than borderline and malignant tumors. The expression of Ki-67 was more in malignant tumors.[15]

V.manu *et al* in 2018 evaluated the expression of p53, p16, Wilms tumor gene (WT1), and Mindbomb E3 Ubiquitin Protein Ligase 1 (MIB-1) index by immunohistochemical (IHC) staining in benign, low-grade, and high-grade serous ovarian tumors. In their study 41 cases of ovarian serous tumors were included (benign serous tumor [n=10], low-grade ovarian serous carcinoma [n=8], and high-grade ovarian serous carcinoma [n=23]). Inference was made that p53, p16, and WT1 showed significantly higher staining scores in ovarian serous carcinoma(high grade than low grade) group than in the benign group ($p < 0.05$). MIB-1 scores were not significant. Conclusion was made that p53, p16, and WT1 were helpful for the subtyping of serous ovarian tumors as low grade and high grade.[16]

Najla *et al* in 2019 conducted a study to distinguish between primary ovarian mucinous tumors and metastatic mucinous neoplasms from the lower gastrointestinal tract, including appendiceal tumors. A combination of PAX8 and SATB2 immunohistochemical stains were used as a diagnostic tool to distinguish between these cases. Immunostaining for SATB2, PAX8, CK7, CK20 and CDX2 was performed on 50 ovarian mucinous neoplasms (OMN), 63 mucinous colorectal carcinoma (CRC), and 9 appendiceal mucinous neoplasms

(AMN).Conclusion was made that PAX8 can differentiate between OMN and AMN with high specifcity but low sensitivity. CDX2 is the most sensitive marker for CRC and AMN, whereas SATB2 has better specificity.[17]

Emma *et al* in 2020 conducted a study regarding hereditary causes of ovarian cancer which included Lynch syndrome, which was due to inherited pathogenic variants affecting one of the four mismatch repair genes involved in DNA repair. In total 261 ovarian cancers were tested and 27 showed mismatch repair deficiency by IHC. Three of 7 with MLH1 loss showed MLH1 promoter hypermethylation, and 18 of the remaining 24 underwent constitutional testing for Lynch syndrome. A further 15 women with mismatch repair proficient tumours underwent constitutional testing because of a strong family history of Lynch syndrome cancers. Pathogenic variants were identified in 9/33 (27%) women who underwent constitutional testing, aged 33– 59 years (median 48 years), including one whose tumour was mismatch repair proficient. Most Lynch syndrome tumours were of endometrioid histological subtype. Their study concluded that tumour mismatch repair deficiency identified by immunohistochemistry is a useful prescreen for constitutional testing in women with ovarian cancer with personal or family histories suggestive of Lynch syndrome.[18]

Lorena *et al* in 2020 found that loss of function in either breast cancer type 1 susceptibility protein (BRCA1) or breast cancer type 2 susceptibility protein (BRCA2) was a major risk factor for epithelial ovarian cancer (EOC) development.[19] BRCA1 and BRCA2 dysfunction, frequently seen in high-grade serous ovarian carcinomas, often results from germline mutations, somatic mutations, and promoter methylation.[20] The main concepts for the study were: ovarian neoplasms, IHC, BRCA1 and BRCA2.Forty-four studies from 925 unique titles were included. A total of 4206 tumour samples were evaluated for BRCA1 and 1041 for BRCA2 expression. Using the cut-off of 10%, 47.0% of EOCs were associated with loss of BRCA1 and 34.5% with the loss of BRCA2 expression. Hence, it was concluded that IHC was effective to detect loss of BRCA1 protein expression in

EOC; however, data on BRCA2 expression were heterogeneous and difficult to interpret.[21]

The most common monodermal teratoma, struma ovarii, usually has an overt follicular pattern and is easily recognized, but recognition of unusual appearances ranging from oxyphilic to clear cell to various patterns of malignant struma may be greatly aided by thyroglobulin or TTF 1 stain.[22] Pseudomyxoma peritonei (PMP) is a condition characterised by mucinous ascites and the presence of multifocal mucinous tumours within the peritoneal cavity.[23] These studies have suggested that in most cases of PMP with concomitant ovarian and appendiceal neoplasms, the PMP is of appendiceal origin (CK7 negative, CK20 positive).[24] Thus, immunohistochemistry plays an important role in the differential diagnosis of the three main categories and some less common ovarian tumors, with the help of recently developed antibodies.[25]

6.3 AIMS AND OBJECTIVES OF THE STUDY

1. To study immunohistochemical spectrum of ovarian neoplasms and correlation with histopathology.

7. MATERIALS AND METHODS

All the histopathologically diagnosed ovarian neoplasms in which IHC studies will be done received in the Department of Pathology, Dayanand Medical College and Hospital, Ludhiana will be included in the study. Slides will be subjected to IHC examination under both low power (100x) and high power (400x)

7.1 Source of Data

This will be a one year retrospective from 1st March 2020 to 28th February 2021 and one year prospective study from 1st March 2021 to 28th February 2022 to be conducted for two years in the Department of Pathology, Dayanand Medical College and Hospital, Ludhiana.

7.2 METHOD OF COLLECTION OF DATA

INCLUSION CRITERIA

All ovarian neoplasms including primary & secondary neoplasms undergoing immunohistochemistry for definite categorization.

EXCLUSION CRITERIA-

All non ovarian neoplasms and any ovarian neoplasms on which immunohistochemistry (IHC) has not been done.

Methodology: IHC staining of slides prepared from formalin fixed paraffin embedded tissue (FFPET) on the BenchMark Classic Automated System (from Ventana). Sections from FFPET biopsies are cut using the microtome at 3-4 micron thickness and mounted onto SuperFrost Plus slides. For each slide, Ventana labels are then printed which include a unique barcode containing all protocol information. The slides are then loaded onto the BenchMark carousel and read by the Ventana Barcode Reader. The automated BenchMark system puts the slides through a series of user-defined de-paraffinization and antigen retrieval steps before commencing with the antibody staining. primary antibody is either applied automatically if in a pre-diluted dispenser or otherwise manually titrated onto the slide. The pre-diluted dispensers of the ultraView Universal DAB Detection Kit then provide all reagents required for staining. The counterstain and post-counterstain comprise

Haematoxylin (cat # 760 – 2021) and bluing reagent (cat # 760 – 2037).

DURATION OF STUDY

This will be two years study, conducted one year retrospective from 1st March 2020 to 28th February 2021 and one year prospective study from 1st March 2021 to 28th February 2022.

OUTCOME

IHC findings of ovarian neoplasms will be documented according to the protocol.

STATISTICAL ANALYSIS

Data will be described in terms of range; mean +/- standard deviation (+/-SD), frequencies (number of cases) and relative frequencies (percentages) was appropriate. All statistical calculations will be done using SPSS (Statistical Package for The Social Science) SPSS 21 version statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

No.

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached herewith.

LIST OF REFERENCES

1. Naik PS, Deshmukh S, Khandeparkar SG. Epithelial ovarian tumors: Clinicopathological correlation and immunohistochemical study. J Midlife Health. 2015;6:178-83.
2. Basu P, De P, Mandal S, Ray K, Biswas J. Study of 'patterns of care' of ovarian cancer patients in a specialized cancer institute in Kolkata, Eastern India. Indian J Cancer. 2009;46:28-33.
3. Sylvia MT, Kumar S, Dasari P. The expression of immunohistochemical markers estrogen receptor, progesterone receptor, Her-2-neu, p53 and Ki-67 in epithelial ovarian tumors and its correlation with clinicopathologic variables. Indian J Pathol Microbiol. 2012;55:33-7.
4. Khan L, Arora A, Agarwal A, Pantola C, Kala S, Rathi RK, et al. Role of Immunohistochemistry in Ovarian Tumors. Journal of Evolution of Medical and Dental Sciences. 2014;3:2814-20.
5. Piek JM, van Diest PJ, Verheijen RH. Ovarian carcinogenesis: An alternative hypothesis. Adv Exp Med Biol 2008;622:79-87.
6. Buchynska LG, Iurchenko NP, Grinkevych VM, Nesina IP, Chekhun SV, Svintsitsky VS. Expression of the estrogen and progesterone receptors as prognostic factor in serous ovarian cancers. Exp Oncol 2009;31:48-51.
7. Hall PA, Levison DA. Review: Assessment of cell proliferation in histological material. J Clin Pathol. 1990;43:184-92.
8. Gursan N, Sipal S, Calik M, Gundogdu C. P53, bcl-2, ki67 li (labeling index) status in benign, proliferative, and malignant ovarian surface epithelial neoplasms. Eurasian J Med. 2009;41:10-4.
9. Richard W. Cartun Clive R. Taylor.Techniques of Immunohistochemistry: Principles, Pitfalls, and Standardization. Dabbs DJ (editor). Diagnostic Immunohistochemistry: Theranostic and Genomic applications; 5th edition. Elsevier: Philadelphia; 2015. P.1-32. & P.695-708.

10. Kandalaft PL, Gown AM. Practical Applications in Immunohistochemistry: Carcinomas of Unknown Primary Site. Arch Pathol Lab Med. 2016;140:508-23.
11. Liliac L, Carcangiu ML, Canevari S, Căruntu ID, Ciobanu Apostol DG, Danciu M, Onofriescu M, Amălinei C. The value of PAX8 and WT1 molecules in ovarian cancer diagnosis. Rom J Morphol Embryol. 2013;54:17-27.
12. Young RH, Scully RE. Metastatic tumors of the ovary. In: Kurman RJ, editor. Blaustein's pathology of the female genital tract. 5th ed. New York: Springer; 2002. p. 1063–101.
13. Young RH, Clement PB, Scully RE. The ovary. In: Sternberg SS, Antonioli DA, Mills SE, Carter D, Oberman HA, eds. Diagnostic Surgical Pathology. 2nd ed. New York: Raven Press; 1994.
14. Ferguson DC, Long DJ, Smith MC. Comparative analysis of Rb1, P16 and ER as diagnostic, prognostic and potential targets for therapeutic agents in ovarian epithelial tumors: an immunohistochemical study of 130 ovarian carcinomas. J Ovarian Res. 2015;8:34
15. Naik PS, Deshmukh S, Khandeparkar SG, Joshi A, Babanagare S, Potdar J, Risbud NS. Epithelial ovarian tumors: Clinicopathological correlation and immunohistochemical study. J Midlife Health. 2015;6:178-83.
16. Manu V, Hein TA, Boruah D, Srinivas V. Serous ovarian tumours: Immunohistochemical profiling as an aid to grading and understanding tumorigenesis. Medical Journal, Armed Forces India. 2018;76:30-6
17. Aldaoud N, Erashdi M, AlKhatib S, Abdo N, Al-Mohtaseb A, Graboski-Bauer A. The utility of PAX8 and SATB2 immunohistochemical stains in distinguishing ovarian mucinous neoplasms from colonic and appendiceal mucinous neoplasm. BMC Res Notes. 2019;12:770.
18. Crosbie EJ, Ryan NAJ, McVey RJ, Lalloo F, Bowers N, Green K, et al. Assessment of mismatch repair deficiency in ovarian cancer. J Med Genet. 2020;2020:107270.
19. Teixeira LA, dos Reis FJC. Immunohistochemistry for the detection of BRCA1 and BRCA2 proteins in patients with ovarian cancer: a systematic review. Clin Pathol. 2020;73:191–6.
20. Vos S, van Diest PJ, Moelans CB. A systematic review on the frequency of BRCA promoter methylation in breast and ovarian carcinomas of

BRCA germline mutation carriers: Mutually exclusive, or not? Crit Rev Oncol Hematol. 2018;127:29-41.

21. Manchana T, Tantbirojn P, Pohthipornthawat N. BRCA immunohistochemistry for screening of BRCA mutation in epithelial ovarian cancer patients. Gynecologic Oncology Reports. 2020;33:100582.
22. McCluggage WG, Young RH. Immunohistochemistry as a diagnostic aid in the evaluation of ovarian tumors. InSeminars in diagnostic pathology 2005;22(1):3-32.
23. Syed A Hoda, MD, Esther Cheng, DO, Robbins Basic Pathology, American Journal of Clinical Pathology. 2017;148:557.
24. McCluggage WG Recent advances in immunohistochemistry in the diagnosis of ovarian neoplasms Journal of Clinical Pathology. 2000;53:327-334.
25. Baker PM, Oliva E. Immunohistochemistry as a tool in the differential diagnosis of ovarian tumors: an update. Int J Gynecol Pathol. 2005;24(1):39-55.

PROFORMA

Sr. No. _____

Name Age/Sex

MRD No. Date

Histopath No. IHC No.

Address

Brief history:

Clinical History

Other (specify):

Past history

Personal history

Family history

- Of any cancer
- Hereditary breast/ovarian cancer
- Lynch syndrome

Reproductive history

Menstrual history

Previous treatment history(surgery/chemotherapy/radiotherapy), if any

General physical examination:

Pallor Icterus Cyanosis Clubbing

Abdomonal examination:

Hepatomegaly Splenomegaly Free fluid

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Investigations:

Haemogram

Urine routine

Liver function tests

Renal function tests

Biochemical/Serological markers

- CA-125
- CEA
- AFP
- LDH

Radiological findings:

- USG findings
- CT scan findings
- MRI findings
- PET scan findings

Ancillary Studies

- BRCA1 mutation testing, if any:
- BRCA2 mutation testing, if any:
- DNA mismatch repair enzyme studies, if any:

Gross examination

Type of specimen:

- Trucut / incisional biopsies from ovary/ovaries
- Excisional biopsies/specimen

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Total hysterectomy and bilateral salpingo-oophorectomy

Bilateral salpingo-oophorectomy

Right salpingo-oophorectomy

Left salpingo-oophorectomy

Salpingo-oophorectomy, side not specified

Right oophorectomy

Left oophorectomy

Oophorectomy, side not specified

Other (specify): _____

Description of the gross (including site and external features)

Specimen integrity

Specimen Integrity of Right Ovary

- Capsule intact
- Capsule ruptured
- Fragmented
- Other (specify):

Specimen Integrity of Left Ovary

- Capsule intact
- Capsule ruptured
- Fragmented
- Other (specify):

Specimen Integrity of Right Fallopian Tube

- Serosa intact
- Serosa ruptured
- Fragmented
- Other (specify):

Signature of Candidate **Signature of Supervisor**

Specimen Integrity of Left Fallopian Tube

- Serosa intact
- Serosa ruptured
- Fragmented
- Other (specify):

Tumour site

- Right ovary
- Left ovary
- Bilateral ovaries
- Ovary, laterality cannot be determined:
- Right fallopian tube
- Left fallopian tube
- Bilateral fallopian tubes
- Fallopian tube, laterality cannot be determined:
- Right tubo-ovarian
- Left tubo-ovarian
- Bilateral tubo-ovarian
- Tubo-ovarian, laterality cannot be determined:
- Primary peritoneum
- Other:

Ovarian Surface Involvement

- Present Specify laterality:
- Absent
- Cannot be determined:

Fallopian Tube Surface Involvement

- Present Specify laterality:
- Absent
- Cannot be determined:

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Size

- Tumor Size (in centimeters)

Cut section

- Cystic
- Solid
- Unilocular
- Multilocular
- Contents with consistency- serous/mucinous/hemorrhagic
- Colour
- Fibrosis
- Calcification
- Any other

Implants

- Not sampled
- Not identified
- Present (specify sites)

Lymph nodes (if present in the specimen)

- Involved
- Uninvolved
- Cannot comment

Microscopic examination:

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WHO Grading System

G1: Well differentiated

G2: Moderately differentiated

G3: Poorly differentiated

GX: Cannot be assessed

Two-Tier Grading System

Low grade

High grade

Other (specify):

Not applicable

Provisional histopathological diagnosis:

IHC Markers: Cytoplasmic Nuclear Membranous Intensity Focal Diffuse

ER

PR

CK7

CK20

Pax-8

HMWCK

EMA

CEA

CA 125

WT1

Beta- catenin

Vimentin

GATA 3

p53

Napsin A

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Inhibin

Calretinin

SF-1

FOXL2

PLAP

CD117

AFP

Glypican-3

hCG

SALL4

Chromogranin

Synaptophysin

NSE

CD56

CD30

P16

Rb1

Ki-67

MIB-1

SATB2

CDX2

Any other

Immunohistochemical findings:

Final histopathological findings:

Signature of Candidate **Signature of Supervisor**